

Waiting for Lord Rothschild

A YEAR ago, the present British government was boasting of how it would differ from its predecessor by being good at management and by conducting its affairs openly, with ample discussion with interested parties before important decisions were arrived at. Nobody will forget that in the past year, the government has had a good deal on its mind. With luck, it may scrape into the European Communities, but Northern Ireland is likely to be a more durable distraction. That said, however, it is more than a little hard to understand precisely how the government hopes to rescue its reputation in its dealings with science, scientists and higher education. Certainly there is no sign of what used to be called open government. There is precious little evidence of the good management of which the government used to boast. If the issue were merely the government's reputation, of course, there are many who might consider that a fall from grace would do very little harm. The sad truth, however, is that several important matters are now being held up by the slowness with which urgent decisions are being made.

The way in which the Dainton report on the organization of basic science in Britain has vanished into limbo (see *Nature*, **232**, 287; 1971) is only one sign of the malaise. Mrs. Thatcher, the Secretary of State for Education and Science, has been telling the House of Commons for months that she would be able to make a decision on the future of the support for universities only after the University Grants Committee has completed its review of higher education. Not until the autumn, and only then with luck, will the first fruits (if that is the word) of Lord Rothschild's review of public expenditure on research and development as a whole begin to appear. And no doubt months will go by thereafter before all the uncertainties are resolved. Is it really now the government's intention to abolish the Atomic Energy Authority? What will happen to the research councils? Are they to be more closely integrated with each other and with higher education, or to be recreated in a new no man's land in between higher education and public service proper?

While no decision has been made and all the relevant documents are kept still unpublished, it is no wonder that there is widespread anxiety about the recipes for change which the government is devising. Certainly the way in which senior government scientists have been offered no pay award this year has been interpreted by many as a sign that there are harsher rods in pickle, and no amount of exhortation about the objectivity of the Pay Research Unit will convince the people concerned that their prejudices are misplaced. Most probably, people's worst fears will turn out to be illfounded, but that is only another way of saying that the government would have done a considerable public service if it had simply chosen to publish more of the raw material on which its decisions will eventually be made. If the Select Committee on Science and Technology wishes to redeem its most recent error—the scheme for setting up a special government

agency to keep an eye on the growth of the British population (see *Nature*, **231**, 140; 1971)—it could do worse than go after Mr Heath's government for these inexcusable omissions and delays.

There are also policy decisions to be made, the simplest of which is one that might have been a gargantuan task as recently as a year ago—the refashioning of the machinery for administering what the government spends on basic research. This is what the Dainton report is all about. The questions with which it no doubt deals go deeper than how most efficiently to deal with the spending of £115 million a year (the present rate of expenditure) on university research and supporting facilities for university research in Britain and abroad, together with the miscellaneous collection of research projects more directly aimed at practical problems which are supported on the shoulders of the Agricultural, Medical and Natural Environment Research Councils.

In the first place, there is the question of how the research councils should be related to the other sources of university funds. For the past five years, it has been supposed that the object of the research councils should be to encourage in the pattern of university research a diversity which the necessarily egalitarian procedures of the University Grants Committee cannot provide. The policy has been successful even though there is a chance that pure reason by itself might have worked wonders in some areas of research. Yet it is at least worth asking the question, in present circumstances, whether the research councils would not be more effective than at present if they were less directly concerned with the bread and butter of higher education, especially the support of postgraduate students, and more concerned to be highly discriminating grant-givers.

Next comes the now more familiar question of what should be the relationship of the research councils to each other. Is it really necessary to have four research councils working in the natural sciences, with another in the social sciences as well? Understandably, the people who operate the present machinery are always eager to describe its virtues, yet it remains a fact that important fields of research—whole organism biology, for example—have frequently fallen between the fingers of the two or three councils chiefly concerned. There is also the embarrassing conflict of philosophy between councils which consider that their chief obligation is to the universities and those who consider that they must “get things done”, usually by the creation of intramural laboratories.

Over all these questions lies the crusty shadow of what is called the Haldane principle, the doctrine laid down by Lord Haldane during the First World War that there should be a kind of tension between those carrying out research within the government and those government departments likely to make the greatest use of the research. This is the spirit in which, first of all, the National Physical Laboratory was established as a kind of custodian of the then government's scientific conscience. At



the time, the Haldane principle may have been a necessary simplification. After all, when research was still a novelty, there may have been good practical reasons for not spreading it too thinly. Now, however, the Haldane principle has outlived its universal influences. Good government departments—those concerned with transport and agriculture, for example, are ready enough to regard research as a necessary part of the machinery of government. Others, less imaginative, shelter behind the Haldane principle, which has become to them an excuse for doing comparatively little. It is no accident that the Department of Health and Social Security and the Medical Research Council between them carry out much less research of the kind likely to yield practical benefits in the operation of the health service than circumstances require. In short, this by itself is a sufficient proof that the time has come to abandon Haldane. Whatever Dainton may have to say on the relationship of the research councils to the universities and to each other, the chances are high that he will have recommended a shading of this ancient doctrine.

The government's relationship with industry is a continually vexed question. Over the years, the government has accumulated a whole string of anomalous policies. The research associations, the darlings of the early fifties, are now considered pariahs. The National Physical Laboratory, intended in an earlier age to stimulate industrial innovation, has settled down to quite a different task. The recommendations of the Trend committee in the early sixties, echoed by Mr Anthony Wedgwood Benn in his scheme for reorganizing his research and development establishments, that there should be independent research and development authorities for different fields of industrial activity, is also now a dead letter. In circumstances like these, it must be exceedingly tempting for somebody like Lord Rothschild to seek an entirely novel formula for helping to stimulate industrial innovation by the sensible use of public money.

By good chance, Lord Rothschild should know that there are many ways in which the job could be done. One of the most important is to find some way of helping to make it seem to commercial enterprises that spending money on research and development is in the long run profitable. How is this to be accomplished? One necessary change of direction is that companies should be persuaded not merely that the manufacture of a successful typewriter, for example, may be more important than the manufacture of an unsuccessful aircraft engine but that research and development have as important a contribution to make to the former as to the latter. Exhortation might help, but the precedents for this are few. Taxation (or the amelioration of it) might also help. Government purchasing, by selectivity and even its willingness to go abroad, could have an important influence on the zeal of British enterprises. In the long run, however, example is what matters most.

Should not Lord Rothschild in his Jovian view of British science examine one field from which his predecessors have usually been excluded, either by design or cowardice—the nationalized industries? At first sight, at least, too many people are doing far too little research in the nationalized industries, even though these are publicly owned. The cost of this neglect is well typified by the scandal of the broken down generating sets in the United Kingdom two years ago. To bring about a better

climate for research and development in this important field would be valuable in itself, an important example to other industries and also a way of using a stock of talent which seems to have become an embarrassment to the politicians.

Higher education is also being quickly muddled, not so much through malevolence as indifference. Two weeks ago, Mrs Thatcher announced in the House of Commons her decision that the polytechnics would be given extra funds to help with their development, a step which in itself is wise and even humane, for the polytechnics have a long way to go to whatever goals they and Mrs Thatcher, in their several ways, consider to be justifiable. The trouble is that nobody is quite sure what strategy the government has for the development of the polytechnics and for their relationship with the universities on the one hand, and the colleges of education on the other. Is it, as it might be, that pushy polytechnics will in future be encouraged to usurp the position of the weaker universities in the academic pecking order? Is it, alternatively, that Mrs Thatcher was trying her best to make a virtue of necessity in much the way Mr Anthony Crosland was forced to make the best of a *fait accompli* when he first argued the case for what is called the binary system of education in 1964? Here again, perhaps, Mrs Thatcher is being compelled to wait for the report of yet another committee—Lord James's inquiry into the education of teachers. The trouble is that by continuing to spend public money on higher education without doing the government's essential job in the formation of policy, Mrs Thatcher is creating a set of circumstances from which nothing but disappointment can spring.

This is one field in which the Rothschild inquiry could help to unlock the log-jam in which important decisions seem to be imprisoned. It is only fair to say, however, that his influence will be diminished if he cannot find some way of simplifying and making intelligible the machinery at present used for making the decisions that seem to elude him. Over the years, the decision-making apparatus has grown by accident. The research councils are said now to know more clearly where they stand than under the previous government, but there is a fuzzy line between them and the University Grants Committee alongside them and the Council for Scientific Policy above them. But in any case, the council is merely advisory, as was Sir Solly Zuckerman's old Advisory Committee on Science and Technology, a body apparently distinguished by the irregularity with which it met. Scientific advisers abound—Sir Alan Cottrell in the Cabinet Office has replaced Sir Solly Zuckerman, who nevertheless has stayed on as an occasional consultant. The Ministry of Defence has its own apparatus for devising policy on research and nobody quite knows how all of them are subservient to Lord Rothschild's office, the nearest thing in Britain to the Office of Management and Budget in the United States. The consequences of this complicated and ill-defined structure are apparent in complaints like this. Although it is by now apparent that the British government habitually loses a great deal of decisiveness by its failure to be open with its constituents, it is also true that in the management of its policy on research and development, the machinery that exists is a hindrance, not a help. If ever the tablets on which Lord Rothschild is supposed to be working are brought down from the mountain, this is the first thing to be written on them.

Ducks and Drakes

It is to be hoped that only pre-Keynesian bankers will be dismayed at the discovery that it has been necessary to restrict the convertibility of the United States dollar. Elsewhere in the world, there is plenty of recent experience to show that the most upright and high-minded people can survive the shame even of devaluation, a much more conspicuous way of passing over the claims of creditors than the package announced earlier this week in Washington.

To be sure, there are two other components of recent memory that will make those outside the United States uneasy. First of all, draconian as Mr Nixon's proposals may appear, they resemble all too closely the kinds of stratagem that British Chancellors of the Exchequer have been forced to use in the past few years in the attempt to avoid full-scale devaluation, so that even those who wish Mr Nixon well may be tempted to hedge their bets by converting whatever dollars the system will now allow. The second vivid memory is the histrionic quality of what is called the crisis through which it is now said the world is passing. If reason has any place in monetary affairs at all, events of the past week are most of all remarkable not because it has been necessary to hedge about the relationship between the dollar and other currencies but because the United States has been able to keep on buying gold at one ounce for \$35 for more than a quarter of a century. How can it be that a numerical relationship established in 1946 at a remote village in New Hampshire should have persisted so long?

The first thing to be said is that the relationship between gold and the dollar has been in itself artificial. President Franklin D. Roosevelt is said to have left the gold standard in the early thirties, but nobody really knows what that means. Each decade there seems to be another crisis of conscience in the United States, and each time there seems to be a reaffirmation of the view that gold and the dollar must (at some price) be at one. The affection of the United States for gold is, of course, a powerful stimulus of the gold-mining industry but in reality the objective is not so much to provide an absolute monetary standard but rather to relate the prices paid in dollar bills for commodities imported or exported to a quantity of material which can be reckoned to have a fixed value on a time scale which is longer than the interval during which commercial transactions between nations are settled. In other words, the function of the relationship between the dollar and the price of gold has been to provide a yardstick by means of which currencies might be converted. Its disadvantage has been that stocks of gold, sometimes many times the nation's Gross National Product in value, have also been given their face value.

What can scientific research and development contribute to a solution to this problem? The most obvious device would be relating the value of the dollar not to gold but to some naturally radioactive material, preferably one with a lifetime comparable with the lifetime of a human generation (so that hoarders would not feel too cheated) but not so great that jackdaw nations could dominate the international monetary scene to a degree not matched by their current economic performance. (In some quarters, it will be a shock to know that strontium-90 appears to have a suitable lifetime.)

These, however, are devices which share with the

monetization of gold the defect of being symbolic. Why not instead seek means by which currencies are converted into each other at rates determined by the current economic performance of the countries concerned but smoothed out over an interval of time (say three months) so that commercial transactions would not be seriously impeded? By now, the economic textbooks are thickly peppered with proposals of this kind, some of them known by the unedifying name of the crawling peg. It is almost beyond belief that in a world which chooses to rack its conscience regularly on the issue of whether the profession of science is sufficiently responsive to social needs, economists and bankers should be allowed such licence as they assume in the handling of the international exchanges. At this point, few people may be able to guess how much gold to swap for dollars three months from now, but it is a near-certainty that by then each ostrich will once more have buried his head firmly and, he hopes, permanently in the sand again.

100 Years Ago



CLIFTON COLLEGE SCHOOL OF NATURAL SCIENCE

The accompanying is one of these fortnightly papers :—

MAGNETISM

1. Soft iron can never be permanently magnetised, yet a piece of soft iron in contact with a magnet becomes a magnet. Why?
2. What do you understand by *coercive force*, and magnetic saturation?
3. How is magnetism influenced by heat?
4. Mention the substances which are attracted by a magnet in addition to iron.
5. State one or more of the methods by which steel bars may be magnetised.
6. What is the *declination* or *variation* of the magnetic needle, and the present extent of it?

CHEMISTRY

a. For First and Second Sets, Modern Side only.

1. Mention the oxygen compounds of phosphorus, and the action of water upon them.
2. Give an account of arsenicum and its chief characteristics.
3. What are the constituents and characteristics of arseniuretted hydrogen?
4. What is "white arsenic," and how may it be prepared?
5. You are given a liquid suspected to contain arsenic; by what means would you examine it?

b. For all other Forms.

1. Ammonia gas, and hydrochloric acid gas, are brought into contact: what is the resulting compound, and to what may it be compared?
2. What is *ammonium*? Describe the formation and appearance of ammonium amalgam.
3. What do you know of chloride of nitrogen?
4. What is nitric acid, and by what means may it be procured?
5. State the action of nitric acid upon metals,—copper, tin, antimony,—and the general tendency of the acid.

From Nature, 4, 329, August 24, 1871

OLD WORLD

CENSUS RETURNS

Malthus Fulfilled

PRELIMINARY returns now published suggest that the population of the United Kingdom is growing less quickly than was expected as recently as 1968 (*Census 1971 England and Wales. Preliminary Report*. HMSO, £0.60). The first figures show that in April this year, the population of the United Kingdom was 55.35 million, an increase of 2.64 million or 4.9 per cent since the previous census in 1961. If this preliminary figure is to be relied on, it suggests that there has been no net growth of the population of the United Kingdom since 1968 when, in evidence to the House of Commons Select Committee on Science and Technology, the Government Actuary in the Registrar-General's Office quoted forward projections of the population with 1968 as base year with an actual population of 55.4 million. At that point, it was estimated that the population of the United Kingdom would grow more or less monotonically by about 350,000 a year until 1980. If the growth seems not to have materialized, it will invalidate either the forward projection of the British population or the method used for counting it. For what the figures are worth, the 1971 census suggests that the population of England has risen by 5.4 per cent, that of Wales by 3.0 per cent and that of Scotland by a mere 0.9 per cent. It is something of a surprise that over the decade, Northern Ireland should have the highest growth rate at 6.8 per cent.

There are few surprises in the report, although there are shifts of emphasis from 1961. The fastest growing region in the ten years was the belt from the North Midlands through Leicestershire and Peterborough to the Solent, which coincides with a slackening growth rate in the home counties. A number of local authorities have roughly doubled their population in the past ten years, several in the belt from the Midlands to the Solent.

Coinciding with the drop in the south, West Suffolk and Huntingdonshire become the fastest growing counties with increases from 128,918 to 164,201, and 159,175 to 202,337 respectively. Essex has the biggest single population leap—now 1,353,564, a gain of some 250,000—mostly overspill from London.

The figures also indicate a draining away of population from the centres of large cities—Liverpool shows a loss of 20.4 per cent over the ten years and Manchester 19.9 per cent. Although Greater London has the highest net loss of 613,429, as a percentage it is only 7.9 per cent. All seven of the largest

cities in England had population drops. In the conurbations, however, the drop is less marked—on Merseyside for instance it is only some 8.8 per cent—which suggests that people are moving into the suburbs and surrounding towns of large cities.

The population in the extreme North of Britain decreased, with Lancashire, Cumberland and Northumberland all returning figures lower than in 1961, and Durham showing the smallest percentage growth of any county.

Wales still claims the most thinly populated areas of either country, with Montgomeryshire, Merionethshire and Radnorshire not only the least populated counties but also those with the lowest density of population per hectare. The population in the ex-coal valley of the Rhondda fell while the population in the Welsh urban areas fluctuated—Cardiff and Merthyr Tydfil fell whereas Bangor and Swansea grew in numbers.

SCIENTISTS' PAY

Tribunal Tribulations

THE Institution of Professional Civil Servants and the Civil Service Department presented their respective cases to the Civil Service Arbitration Tribunal on Thursday August 12. This was the first time that the two sides had come together since negotiations were broken off on July 2.

The IPCS entered the tribunal riding high on the success of their protest meeting at the Central Hall, Westminster, two days earlier when more than 3,000 scientists from all corners of Britain came to support the institution's case. The Civil Service Department has remained unmoved by all the protest meetings that have been going on since early in July and its offer and the arguments that substantiate it have remained unchanged.

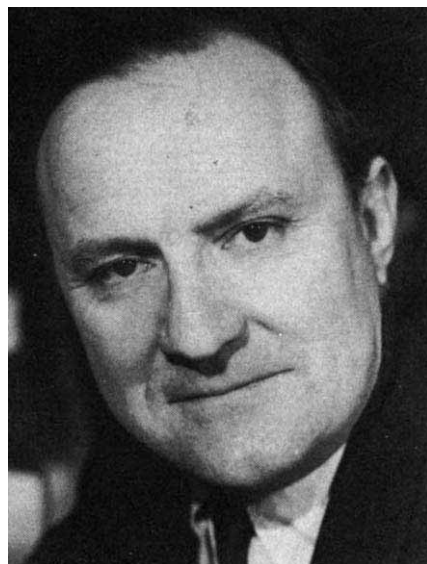
The substance of the government's offer to more than 17,000 scientists, was given in detail in *Nature*, 232, 434; 1971, together with the IPCS's counter claim. The government offered no increase to the higher grades—Principal Scientific Officers, Senior Scientific Officers, Chief Experimental Officers, Senior Experimental Officers and Experimental Officers—and only a small increase to the other scientific grades well below that demanded by the institution. The attitude of the IPCS to this offer was shown in their submittal to the tribunal which states, "members are bitterly resentful of an 'offer' which gives no increase to many, and little to others at a time when the cost of living has risen substantially,



Mr William McCall, General Secretary of the Institution of Professional Civil Servants.

and when other groups of employees in the public and private sectors have received substantial increases".

The Civil Service based its offer on the result of an independent pay research inquiry into the salaries of scientists both inside and outside the Scientific Civil Service, whereas the IPCS would have liked greater emphasis placed on internal relativities within the Civil Service. The government made its position clear in its submission. "The Official Side does not accept that it is necessary, or that it would be appropriate, to resort to horizontal relativities as a primary or even a major consideration in determining the pay of the scientific grades on this occasion



—Photograph by Mark Gerson, FIIP, ARPS.

Rt Hon. the Earl Jellicoe, Minister in charge of the Civil Service Department.

... we are satisfied that the comparisons established by the (Pay Research) Unit are fair and accurate, and that they provide solid evidence on which to base the pay of the scientific grades".

The IPCS countered this by saying that "Pay Research provides an inadequate and unreliable basis for the determination of pay of scientists in the Civil Service because (1) of the quite different circumstances relating to the aims, functions, organization and staffing policies between research and development in government and in industry; and (2) the pervasive influence of the government (by far the largest single employer of scientists) on the pay of scientists in industry vitiates fair comparisons. The institution therefore considers that the pay of scientists should continue to be based solely on internal relativities."

These statements emphasize the extent of the differences between the parties. The institution pressed for the use of internal relativities to determine salaries and advanced several arguments that purported to show that pay research has several shortcomings when used in the present context. These arguments were chiefly based on the different career patterns of the government scientist and the scientist in industry. Among other factors, this results in significant differences in the ages of people doing similar jobs; for example, the equivalent of the Principal Scientific Officer in industry is nine years younger than his counterpart. The Civil Service tribunal announced their decision on the pay of government scientists on Wednesday. The overall result is a compromise between the increases asked for by the IPCS and that offered by the Civil Service Department. There will be an increase of 5% to all those classes not offered anything in the original offer. Mr. McCall described the award as deplorable.

head the team, and a company spokesman said on Tuesday that Dr Fairhurst will be involved as an individual and that the company will not be directly involved.

The commission's report sets out the series of events that led to the tragedy on October 15, 1970, when 35 people lost their lives. A gap of several inches was found between sections 10 and 11 of the west side of the bridge when they were fitted together, and the report states that difficulty in getting the two half girders to the correct relative position "without doubt was due to the fact that the camber curves on the two halves were different not only in amplitude but in the shape of the curve, so that even when connexions had been made at a number of diaphragms it was still necessary to use large forces to make the remaining parts fit."

The large force in this case was applied by means of 80 tons of concrete blocks raised onto the bridge. On September 9, 1970, a buckle was observed and the report says "there can be no doubt that the act of adding the kenteledge"—that is the concrete blocks—"was the precipitating cause of the buckle. . . . The buckle was a clear indication that partial failure of the structure had occurred. The margin of safety against complete collapse must then have been small".

The collapse occurred after an attempt to straighten the buckle on October 15. Previously a buckle had appeared in sections 8/9 on the east side of the bridge, and this had been successfully dealt with in a similar way to the ill-conceived sequence of events that took place on sections 10/11 on the west side. The objective was to remove a series of bolts and so alter the distribution of stress in the buckled structure. The commissioners sum up what followed by saying "... a dramatic change took place. First, the vicious buckle, which up to that stage had been limited to the inner and upper panel, spread into the adjacent two upper panels. This was accompanied by the buckling failure of the upper part of the inner web plate." The report goes on to say "from that time onwards the north half span had inadequate strength to sustain its own weight, and only survived because it was able to bear down on to the south half through the interconnected transverse diaphragms." The collapse of the bridge occurred 50 minutes later which the commissioners feel was a surprisingly long time in the circumstances, and they suggested that "... a small increase in safety margin might have made all the difference".

The plans and calculations of Freeman, Fox and Partners come under close scrutiny in the report, which says that "the calculations contain a great many errors of arithmetic and of

engineering principle and these have gone unchallenged until this commission". The commissioners also stated that "they could not agree with Freeman, Fox and Partners' witnesses that "the design, as it now is, is unquestionably sound". Perhaps the most damning criticism is the following quotation from the report: "We reject ... claims of non-culpability by Freeman, Fox and Partners, and find it hard to believe that those who made such claims can themselves believe them to be true". The report goes on to say "... a basic cause of the tragedy ... was the design inadequacies which led to the safety margins being much too low and certainly lower than the specified values".

Freeman, Fox and Partners in their London office are silent about the report, although Sir Ralph Freeman, one of the senior partners, has been reported in a speech from Melbourne as saying that he categorically denies that the design of the west gate caused or contributed to the collapse. Sir Ralph also stated that he felt that none of the serious allegations made against his firm was well founded.

Indeed the Royal Commission's report and conclusions are the work of three men—Sir Hubert Shirley-Smith, Mr Justice Barber and Professor Bull—and there will be many differing views and opinions on the facts. It is, however, gratifying that a full report has been published. Although a bridge with a similar design collapsed at Milford Haven in June 1970, the whys and wherefores have yet to be made public.

The aspect of this disaster and report which will be of most concern to engineers in Britain is whether it will have any effect on the ability of British firms to bid for contracts abroad. A spokesman at the Institution of Civil Engineers said this week that he did not believe that the report would have any adverse effect. Only time will tell whether this is so.

BOX GIRDERS

Yarra Disaster

THE report of the Royal Commission into the lower Yarra river bridge disaster, published in Australia last week, has apportioned the blame for the disaster among the consulting engineers, the contractors and the bridge authority. The direct result is that the joint consulting engineers Freeman, Fox and Partners of London, and Maunsell and Partners of Melbourne, have been dismissed. To complete the bridge, the Lower Yarra Crossing Authority has instead appointed a team of engineers under its direct control. Dr W. A. Fairhurst, of W. A. Fairhurst and Partners of Glasgow, will

ATOMIC ENERGY

Aldermaston March

THE Executive Committee of the British Society for Social Responsibility in Science has come out against the decision to transfer the Atomic Weapons Research Establishment at Aldermaston from the UK Atomic Energy Authority to the Ministry of Defence. In a statement issued earlier this week, the committee says that it is opposed to any steps to increase the size of the British defence establishment. It also argues that there are potential dangers in giving a single minister responsibility for the manufacture of nuclear weapons and for

planning the strategy for using them. The statement goes on to say that under the new arrangements, it will be hard to encourage the recent tendency to divert the energies of the Aldermaston establishment to civil work, and that the publication of results not necessarily of military importance will now be impeded. It singles out for special mention the seismologists at Aldermaston who may be less valuable members of the British scientific community after being transferred to the Ministry of Defence. The committee complains that Mr John Davies, the Minister at the Department of Trade and Industry, has been "guided solely by administrative convenience" in accepting the recommendations of the Rayner committee that Aldermaston should be transferred to the Ministry of Defence, and asks him to change his mind before it is too late.

The Atomic Energy Authority confirmed earlier this week that the seismic unit at Blacknest, Aldermaston, is indeed to be transferred to the Ministry of Defence. Some of those connected with the work of the unit are confident that the transfer will entail no impediment to the free dissemination of the results of the work not directly of military significance. If there is anxiety at Aldermaston, it consists more of a fear that the Civil Service proper will be a less stimulating environment for creative work than the Atomic Energy Authority has provided. A more sombre speculation now coming to the surface is that the decision about Aldermaston, following as it does on the separation of those parts of the Atomic Energy Authority responsible for the manufacture of fuel elements and nuclear fuel, and also radio-isotopes, has left the government with very little option but to abolish the Atomic Energy Authority as such and to set up the Atomic Energy Research Establishment at Harwell as a self-contained concern as free to go its own way as any government establishment can hope to be.

FOUNDATIONS

Drawing in of Horns

THE Smith Kline and French Foundation, one of the smallest and newest of the sources of scientific funds in Britain, has been forced by rising costs and encouraged by recent successes to modify its policy on grant-giving. In the eighth Annual Report, now published, the foundation says that it will in future increase the maximum for an urgent grant from £500 to £700, even if this means that there will be less to spend on more deliberate applications of somewhat larger sums. The foundation has been spending close on

£25,000 a year for the past eight years, and specializes in comparatively small equipment grants, of which eighty-one were awarded last year.

The foundation, whose trustees are Professor F. G. Young, Professor D. A. K. Black, Dr W. A. M. Duncan, and Professor Sir Ashley Miles, was set up in 1961 to dispose of funds donated by Smith Kline and French Ltd, principally for research with a medical bias. The grants, which do not exceed £2,500, are made to individuals working in universities, hospitals or technical colleges, and are most often spent on items of equipment. Ninety per cent of the grants in 1970 were to new applicants, who are given priority over applicants who have received grants before.

The foundation aims to provide for research which could not expect help from public funds, which is presumably the reason for the virtual absence of the two great medical fields of cancer and immunology from the list of research projects assisted in 1970. Five of twenty-eight recipients are working on various cardiovascular problems, but otherwise the range of fields covered is extremely heterogeneous, extending over the role of dopamine in locomotor control, endocrine function in sleep and the biosynthesis of mycobactins.

CONSERVATION

Royal Society at Aldabra

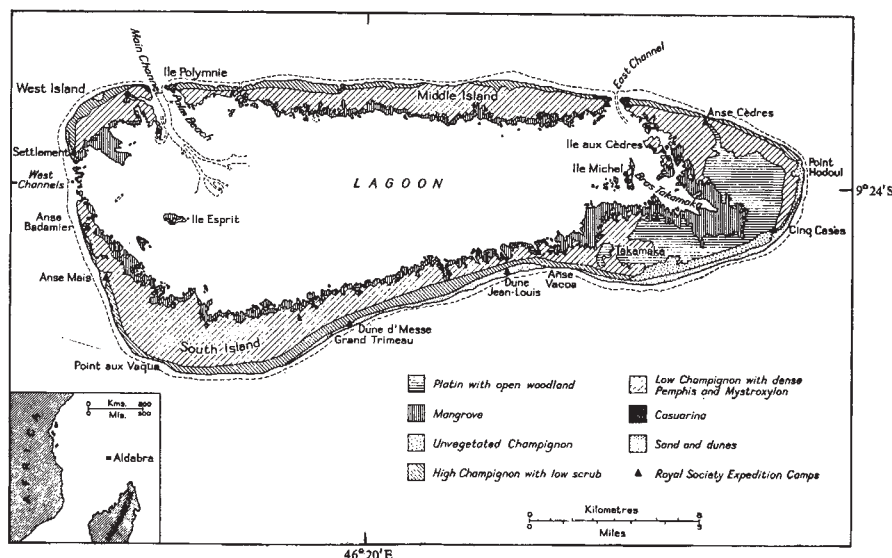
A SAFE future for the Aldabra atoll seems to be assured at last. The Royal Society has bought a fourteen year lease of this unique group of coral islands in the Indian Ocean and will pay only a nominal rent to the Commissioner of the British Indian Ocean Territory.

The Aldabra atoll is an oval ring of inhospitable coral divided into four

principal islands surrounding a shallow lagoon; it is 34 km long and 14 km wide and lies northwest of Madagascar. The future of the atoll was hotly debated in 1967 when the British government was considering a proposal that it should be developed for defence purposes. The Royal Society, the United States National Academy of Sciences and the Smithsonian Institution all expressed grave concern at the time that such activities would seriously threaten almost the last natural home of the giant land tortoise (*Aldabrachelys gigantea*) and the flightless rail (*Dryolimnas cuvieri*) among other species.

At the end of 1967, the British Government abandoned a plan to build a military airfield and the Royal Society went ahead with its long term research programme which is directed by a committee under Professor T. S. Westoll of the University of Newcastle upon Tyne. The first step was the construction of a research station which was completed in June this year at a cost of £50,000. It includes a laboratory building and accommodation for a permanent staff of four, wives included, and for six visiting scientists. Although the station was principally funded by the Royal Society's grant from the British Government, United States National Academy of Sciences contributed \$12,000 for the visiting scientists' accommodation and the World Wildlife Fund donated £2,900 for the purchase of a motor launch. Two-thirds of the £7,500 which the society has paid a Seychelles company for the lease was given by Mr Peter Cadbury but the day to day running of the research activities on the atoll is to be paid for out of its covenant grant. It has been costing about £30,000 a year.

Although the present lease expires in 1985, with the option of renewal for a



The Aldabra atoll.

UNITED NATIONS

Doom-Watcher

SUGGESTIONS that the United Nations should play a more vigorous part in dealing with natural disasters have now resulted in a resolution of the Economic and Social Council of the United Nations, adopted at the meeting in Geneva at the end of July, which spells out a few practical steps that might be taken. The resolution will be put forward at the next General Assembly in New York. Its chief proposal is the appointment of a man whose job would be the coordination of disaster relief, at least so far as the various organizations of the United Nations are concerned. The idea is that the disaster relief coordinator should have a small independent office at the United Nations, and that he should be equipped not merely to spend money contributed for disaster relief by governments and other organizations, but also to provide technical assistance and, where appropriate, research on the prevention or at least the prediction of natural disasters of various kinds.

Although the new proposal should go a long way to provide a more easily identifiable centre within the United Nations at which disaster relief could be organized, it falls short of the more ambitious suggestions which have been made in the past that the United Nations should, for example, be equipped with some of the materials which have been shown to be valuable in recent disasters—helicopters chief among them. Instead, the Economic and Social Council has suggested that potential donor governments should let the disaster relief coordinator know in advance what kinds of facilities and services they might be able to provide.

further twenty years, a spokesman for the Royal Society emphasized this week that the society's interests are chiefly in the scientific research which can be carried out on Aldabra and that after the period of time considered necessary for the completion of the research programme, the society would hand over the lease to a conservation body.

The principal aim of the research is to understand as completely as possible the structure and function of an elevated limestone island ecosystem. Much of the groundwork was carried out during the expedition to Aldabra which the Royal Society mounted in 1967 when

there was an imminent danger of extensive changes to the ecosystem. More than sixty scientists have visited the atoll since 1967 and many of these have been supported by the Natural Environment Research Council; the Royal Society, however, maintains its central planning and coordinating role in Aldabra research.

ARCHAEOLOGY

Looting for Museums

from our Archaeology Correspondent

IN the past few weeks, museums and collectors have been alarmed by the discovery of several clever fakes, but in the long run science and scholarship may be more seriously damaged by the increasing flow on to the art market of genuine antiquities derived from illicit excavations. In *American Antiquity* (36, iii; 1971), Robert Adams, Director of the Oriental Institute in Chicago, writes a strongly worded comment on this situation, stressing the increasing scale of looting and the irreparable loss to archaeology: "If we do nothing, we condone these growing outrages by our silence and jeopardize the international progress of our field".

Gun-running, indeed, is not as profitable these days as antiquity-running. It is true that in many nations of the world (although not yet in Britain), archaeological excavation is illegal unless authorized by the national antiquities service and archaeological finds are automatically the property of the state. Moreover in many Near Eastern countries, as well as in Central America, antiquities may only be exported under an export licence. Unfortunately, however, most of the pieces which now command so high a price in the art markets of the world—the Mexican sculptures, the Greek vases, the Iranian bronzes—have been illicitly excavated and illegally exported.

This is, of course, of serious concern, since the importance of such finds is not simply their intrinsic worth or even their beauty but the information which the circumstances of their discovery can yield about man's past. The archaeological interest of a hoard of gold coins in an earthenware pot, for instance, may be the opportunity it offers for dating the pot and hence of building up a ceramic chronology which in turn allows monuments and other finds to be dated: the gold itself may be secondary. All this and much more is lost in clandestine digging, where the associations are never reliably recorded and all the information obtainable by the use of scientific aids in archaeology goes unremarked.

It is widely and increasingly felt that much of the responsibility for the in-

creasing loss of archaeological knowledge through illicit digging must be borne by those museums and private collectors who pay vast sums for unprovenanced antiquities, with no questions asked. In many cases these august institutions are, in effect, knowingly receiving stolen goods illegally exported from their country of origin. Indeed it is not unknown for Classical statues and vases, found in Greece or Italy, to be deliberately smashed by the diggers so that the pieces may be more conveniently exported than would the complete object, and subsequently re-assembled for sale in Switzerland.

The problem has been discussed recently in the context of the "Boston Affair"—not the strangler but the Museum of Fine Arts. The museum, already under a cloud for smuggling into the United States a painting allegedly by Raphael, has also been attacked for obtaining an impressive hoard of prehistoric gold jewellery, obviously from the eastern Mediterranean. The treasure, bought by an anonymous benefactor, is itself regarded by some as at best a collection of un-associated finds put together by an astute dealer and, at worst, a bunch of fakes.

The acquisition rather unexpectedly produced a strong swell of protest in the archaeological world, reported in *Antiquity* (44, 88, 171 and 257; 1970) in editorials by Glyn Daniel. In a sense, the museum was only doing what many others have done. It is ironical, therefore, that the "Pennsylvania Declaration", a somewhat sanctimoniously worded document from the University of Pennsylvania Museum renouncing the intention of buying unprovenanced antiquity (*Antiquity*, 44, 171; 1970), should come from an institution which only recently bought a comparable treasure in very similar circumstances. Indeed, that hoard of gold jewellery from the east Mediterranean seems more probably genuine than the Boston hoard, and it was recently given authoritative publication in an admirable and scholarly article by Dr George Bass (*American Journal of Archaeology*, 74, 335; 1970). Despite its holier-than-thou attitude, the Philadelphia Museum is right. International legislation is needed and, above all, a real public awareness in the purchaser countries that to buy important unprovenanced antiquities is directly to support looting and the destruction of the past.

Every museum and many private collectors have this sort of skeleton in their cupboards—the Elgin Marbles and the Codex Sinaiticus are British examples. Yet the urgent problem is not so much one of restitution as of stopping the looting. That is why it is right to pillory the unhappy authorities of the Boston Museum.

INDUSTRIAL ARCHAEOLOGY

Through the Past Darkly

ELECTRICITY'S past may be preserved in a museum. The museum subcommittee of the Electricity Council meets next week and may recommend that a museum should be established. But it is still a matter for debate. Since December last year, Mr J. P. Tanner, formerly manager of the Northern District of the London Electricity Board, has been asking the area boards for details of equipment in their possession that might be of historical interest. The response has been mixed, but most of the boards have appointed somebody to keep in touch with Mr Tanner and the information he wants is beginning to come in.

It is not yet clear if there will be enough equipment worth preserving, but if there is—as seems likely—a museum is not the automatic answer. Would there be sufficient public interest in such a venture to make it worthwhile? Where would it be? And how would it be financed? All these questions need to be answered.

The site problem could be solved by using an old power station. There are several in London, for example, that are being phased out, but clearly only one complete generating plant and assorted smaller items could be displayed in the space available, and to allow for more than one complete plant would require a very large site. And if the museum were to be open to the public, it would have to be easily accessible. But the cost of a large site near the centre of a city could be excessive. An alternative method would be the continuation of

Mr Tanner's work of compilation and documentation in considerably greater depth, with detailed descriptions of early power stations and equipment put on record, along with accurate models. Films could be made about old generating plants that are still in use before they are phased out and dismantled.

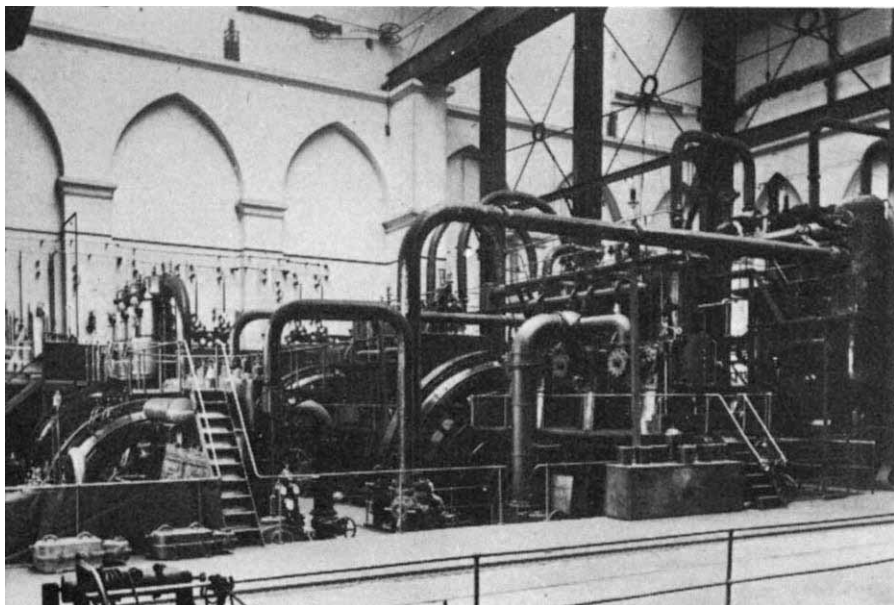
But the basic question to be resolved is for whom this preservation of gleams from the past is intended—the general public or the specialist. A detailed compact record, with models and film, available to only a limited number of people at any one time, would presumably be a more economical operation than establishing a large and costly museum for a possibly apathetic public. The cost of either project would be high, although the museum would probably prove to be the more expensive of the two, and government aid would almost certainly be needed to make either scheme viable.

At present Mr Tanner is based at the Science Museum where Mr Brian Bowers, keeper of the electrical section is advising him. They are not alone in their work for since March 1965 members of the Institute of Electrical Engineers History of Technology Group have invited interested members to send in record cards of existing historical pieces to the group who collate the information and offer it to museums. Until a full assessment of the equipment available has been made, and a decision taken as to the precise purpose of preservation, the best method of preserving the past cannot be decided.

Miscellaneous

BRITISH production of both plastic materials for packaging and aerosol cans is expected to increase by about 15 per cent during 1971 compared with an increase of 20 per cent in 1970, according to a review carried out by Pira, the research association for the paper and board, printing and packaging industries. But the market for glass containers is expected to go up only by 2.5 per cent to 6,400 million items. Sales of packaging materials in 1970 were worth more than £900 million of which £180 million was accounted for by tinplate containers and £120 million by plastic materials. Plastic prices reached their minimum in 1969 and in some cases (notably PVC polystyrene) have since begun to rise. All packaging prices increased during 1970.

THE mirror blank for the 3.6 metre telescope of the Meudon Observatory has now been delivered to the French National Institute of Astronomy and Geophysics. After two years of grinding and polishing, the mirror will form the main part of the largest telescope in Europe, probably in the Pyrenees. Although the new telescope will be a little smaller than the Anglo-Australian telescope (144-inch compared with 155-inch) and that to be installed at Cerro Tololo by the Kitt Peak Observatory (158-inch), the French mirror is, like those of these other modern instruments, made from "Cer-Vit", the material with a low coefficient of thermal expansion that has brought telescopes of 300 inches or more within the range of practical propositions.



These Ferranti Alternators (10,000 volt, 1 megawatt), with a 35 foot flywheel ring, and with armature and crankshaft weighing 225 tons, were installed in Deptford Power Station for the London Electricity Supply Corporation at the turn of the century by Ferranti.

THE Council for Scientific Policy will be joined for the new term beginning in September by Dr S. L. Bragg, Vice-Chancellor elect of Brunel University, lately a research director at Rolls-Royce. The new recruits also include Dr J. G. Collingwood, director of research at Unilever Limited, and Professor Marie Jahoda, professor of social psychology at the University of Sussex. Professor Jahoda should help to introduce the Council for Scientific Policy to psychoanalytical ways of looking at problems, but it may be of more immediate value that in private life she is married to Mr Austen Albu, MP, long a stalwart of the Labour Party's science policy. After all, as everybody knows, the council will need all the political aid it can muster to help it through the months ahead, when Lord Rothschild's pronouncements may be expected to make up in daring for the way in which the promise of them has helped to justify prevarication in Whitehall.

NEW WORLD

NSF and NASA get their Money

by our Washington Correspondent

CONGRESS, on the eve of its summer adjournment, has finally approved appropriations for the National Science Foundation and the National Aeronautics and Space Administration. Both agencies are to receive budgets for 1972 which are almost identical to the appropriations asked for by the Administration. The budgets were contained in a bill allotting \$18,300 million to the Department of Housing and Urban Development, which was passed by the House on July 29, the Senate on August 3 and signed by President Nixon last week. The bill, which is the fruit of much horse-trading in a conference committee appointed to resolve differences amounting to \$224.5 million in the HUD appropriations originally passed by the House and Senate, allocates \$622 million to the NSF and \$3,298 million to NASA for fiscal year 1972 (which started on July 1). The Administration had requested \$623.1 million and \$3,301 million respectively for these agencies.

The National Science Foundation can breathe a sigh of relief that the cut of \$38 million in its budget recommended by the House Appropriations Committee and approved by the House on June 30 (see *Nature*, 232, 9; 1971), has been more than restored by the conference committee. The House Appropriations Committee, under the chairmanship of Edward P. Boland, suggested a budget of \$585 million for the NSF, but the parallel Senate Appropriations Committee set the foundation's budget at \$648 million. Predictably, the conference committee opted for a final appropriation midway between the two.

In its passage through the Congressional mill, the NSF's budget request has been under strong attack both from the Science and Astronautics Committee in the House and from the appropriations committees, its chief complaint being the NSF's new programme of "research applied to national needs" (RANN). The Science and Astronautics Committee stripped \$30.6 million from the \$81 million earmarked for RANN, and redistributed it to the support of institutions and science education. This move was later followed by the House Appropriations Committee, which acidly stated that "the committee will expect the Foundation to utilize the funds included for science education support and institu-

tional support for science as recommended, instead of the diversion of additional funds to basic or applied research", and cut even further the amounts requested for RANN.

The appropriations bill signed last week gives the foundation some \$109 million more than it received in fiscal year 1971, most of the increase being \$40 million earmarked for picking up basic research projects dropped by other agencies. This item is close to the amount requested by the Administration in its budget application, and its main effect will be to carry on projects that would otherwise have to be abandoned under the terms of the Mansfield amendment which effectively requires the Department of Defense to give up basic research not related to weapon system programmes. Other items included in the appropriations are \$99.3 million for science education support, \$28.8 million for institutional support of science and \$26.8 million for summer institutes and other training programmes for secondary school science and mathematics teachers.

In this year's deliberations over the NSF's budget, the usual Congressional mechanism got itself badly out of step, for the appropriations were passed by both the House and the Senate before the funds had been authorized by Congress. What should happen is that the House Committee on Science and Astronautics and the Senate Committee on Labor and Public Welfare between them set upper limits for the foundation's budget and the appropriations committees then set the final budget levels. This year, however, Congress finally agreed to the authorizations the day after the appropriations were sent to the White House for approval, and the House found itself in the peculiar position of authorizing upper limits for expenditure that had already been appropriated.

The chief reason for this state of affairs was that the House Authorizations Committee set an upper limit of \$622 million for the NSF, while the Senate Committee wanted to authorize \$706.5 million. The matter was then referred to a conference committee which eventually agreed to set a limit of \$655 million. The Senate authorization committee, which was under the chairmanship of Edward M. Kennedy, also recommended that the NSF should receive \$907 million for fiscal year 1973, but this was deleted by the con-

ference committee, and in its place was substituted a request that the NSF should provide the Senate Committee on Labor and Public Welfare and the House Committee on Science and Astronautics with a two-year budget projection for fiscal 1973 and 1974.

Although Congress has looked with some disfavour on the NSF's RANN programme, the foundation is pressing ahead with plans to take a closer look at industrial research and in particular at the possibilities for industry/university collaboration in research projects. It has recently appointed a high-level committee under the chairmanship of Mr Jack E. Goldman, vice-president of Xerox Inc, to consider industry/university relations. Initiation of this committee, however, goes back further than the start of the RANN programme, because when Dr William D. McElroy took over the directorship of the NSF in 1969, he proclaimed that more could be done. Dr McElroy began in fact to recruit members for the committee in April, when he sent letters to individuals pointing out that he believes that there is a gulf between the universities and industry which can be bridged with the help of leadership and stimulation from the NSF and inviting them to serve on the committee. Exactly how the committee intends to bridge the gap is as yet unclear, but in view of the harsh words of the House Appropriations Committee on the NSF's stake in applied research, it will clearly have to tread carefully.

Like the appropriations for the NSF, the final appropriations for NASA agreed by Congress fall short of the Administration's request by only a small amount, for the HUD budget that was agreed to last week contained just over \$3,298 million for the agency compared with the \$3,300 million requested. But in this case the House of Representatives managed to agree on authorizations for the agency two days before it passed the appropriations, and in the Senate, a full six days elapsed between authorization and appropriation. Again, the conference committee which settled the difference between the House and Senate versions of the NASA budget came up with few surprises, for it settled on budget for the agency almost midway between the House and Senate appropriations, adding \$26.5 million to the House bill, but removing \$22.6 million from the Senate bill.

There has been some encouragement for the NASA programme for the development of a nuclear powered rocket (the Nerva programme), and \$39 million is specifically earmarked for this project. The Administration's budget had set aside only \$17 million for Nerva, but even the final appropriation falls short by \$11 million of NASA's original budget request. It seems that NASA originally asked for \$50 million for Nerva for the financial year now begun. But when told by the Office of Management and Budget to reduce its overall budget request, the agency pared some of the costs of the Nerva programme. The Office of Management and Budget then seized the opportunity to remove all the funding for the project, and eventually agreed under strong pressure from NASA to restore \$17 million to keep the project ticking over.

Although the appropriations are not usually broken down into separate figures for each project—only a global sum for research and development, construction and management is given—it seems clear that the conference committee has done well by this shuttle programme. The agency has, to some extent, staked its future on the shuttle, allowing the budget for Nerva and the "grand tour" to be reduced to preserve intact the funding for the shuttle programme, and the Administration's budget request contained \$100 million for the programme for fiscal 1972. In spite of a virulent attack on the programme by forces in the senate led by Walter F. Mondale and in the house by Mrs Bella Abzug, Congress authorized \$115 million for the shuttle. Also in favour with congress is the Skylab programme, which received an extra \$15 million from the authorization committee.

Of the total research and development expenditure authorized by Congress, funding for manned flights is expected to consume some 50.7 per cent—the lowest proportion since 1963—due to the near-completion of the Apollo programme.

NASA's budget for fiscal 1972 represents a decrease of \$14.6 million from last year's funding—a drop which was described by Mr Richard Fulton during the house debate on the final appropriations as financially constraining, and likely to lead to cancellation of several potentially rewarding projects. But this did not appeal to Mrs Abzug, who has been seeking for some time to plunge her knife into the NASA budget. She told the house: "There is sad irony in noting that in the same bill providing a total of \$3,206,324,000—for that department (HUD), there is also provided a larger amount—\$3,271,500,000—for the National Aeronautics and Space Administration. Few more abject demonstrations of our misplaced priorities could be provided".

HIGHER EDUCATION

Straws in the Wind

THE Senate went off on holiday on August 6 after doing as much as could be expected of it to win friends among university presidents and faculty. The Senate, like the House of Representatives is looking forward to July 1, 1972, when the legislation now in force and which regulates federal assistance for colleges and universities will expire.

If in due course the Senate is able to reach a satisfactory compromise with the House of Representatives, at present more concerned to help institutions than students, and if, at the same time, it proves acceptable to the Administration, many of whose proposals on higher education have been incorporated into the Senate bill, there is at least a chance that college presidents in the mid-seventies will be able to spend more time on education and less on fund-raising than has been their custom in the recent past. It is, therefore, of some importance that the Administration has let it be known that the \$18,000 million that would be spent under the Senate bill in the three years 1972–75 is an "unrealistic" figure and that Senator Warren G. Magnuson, chairman of the Appropriations Committee concerned, has let it be known that the federal budget would not be able to accommodate such a scale of spending "in present circumstances". In fact, what the Senate proposes is a scale of expenditure roughly three times that at present advocated by the Administration, which has just been awarded a total of \$1,340 million in the budget for the current year for higher education.

The novel features of the Senate bill are that students would be paid a small stipend—\$1,400 a year—and that the institutions which they attend would also receive financial support directly from the federal government. There are also provisions in the bill for supplementary grants to poor students, an echo of the proposal put forward by the Administration. The schemes for student loans at present in force or in preparation would be continued, as would schemes for seeking out particularly students especially likely to profit from higher education. It is also planned that there should be a honeypot of \$150 million from which universities and colleges which find themselves in a plight similar to that of the Lockheed Aircraft Corporation could be helped out. The Senate has also agreed with the Administration that there should be set up within the Department of Health, Education and Welfare two new agencies to be known as the National Foundation for Post-Secondary Education and the National Institute of Education. It is just possible that academic enthusiasm for the Senate's

action will be moderated, at least in part, by a requirement that students receiving federal support should promise not to use the money for purposes which are not strictly educational. A gallant attempt by Senator Birch Bayh to write into the bill a requirement that women should not be discriminated against in higher education was ruled out of order towards the end of the Senate debate.

On student support, the bill lays down that the basic grant per student shall be either \$1,400 or one half the actual cost of attendance at a university, whichever is the smaller. It is also proposed that the amount of the grant should be reduced by the contribution expected to be made by the student's family, calculated on a sliding scale which has yet to be determined but which takes into account such things as the family income, the number of dependents (particularly those in higher education), the capital assets of the student and his family and such unusual expenses as may be occasioned by medical catastrophes. In general, grants will be valid for no longer than four years, but there are exceptions to cater for five-year courses, for supplementary courses and for circumstances in which the amount of money at the disposal of the Department of Health, Education and Welfare is insufficient to meet the demand. The last provision of the Senate bill is held by its supporters to be a device for making sure that the Administration will not be able to skimp on higher education without damaging the cause of poor students to which it professes to be most deeply attached, but the effectiveness of this strategy, attributed to Senator Claiborne Pell, remains to be seen. It is estimated that the total cost of the basic grant programme, will amount to about \$1,000 million a year.

There are also schemes in the new bill for helping poor and other deserving students. These supplementary grants will be administered by institutions. The Senate bill proposes that something like \$200 million a year will be spent in this way, usually in grants not exceeding \$1,000 (except when a student has performed well in the previous academic year). Supplemental grants of this kind will continue for four years or for the duration of an undergraduate course, whichever is the normal practice of the institution concerned. It will be for universities and colleges to select eligible students, but the federal funds available will be shared out among states in proportion to the numbers of full-time students in higher education. The Senate also suggests that \$50 million a year should be transferred to states prepared to operate a student incentive grant programme.

NEWS AND VIEWS

New Ways with Volcanoes?

THE article by Dr David R. Waldbaum on page 534 of this issue seems well designed to put a cat among the geological pigeons. One way and another, many of the processes considered to take place within the crust of the Earth entail a marked change of pressure. This is most obvious when volcanic material reaches the surface from a substantial depth beneath it, but it is now clear that transformations of the same kind must occur when material is added to tectonic plates at mid-oceanic ridges and, conversely, when the edges of the plates are re-incorporated into the Earth's crust at subduction trenches. The question that Waldbaum seeks to answer is whether conventional thermodynamics can be used to predict changes of temperature likely to accompany these pressure changes.

It is only fair to say that the issue is exceedingly complicated, not least of all because of the difficulty of defining with sufficient clarity the conditions under which these thermodynamic changes take place. The nub of Waldbaum's conclusion is that there must be many circumstances in which a decrease of the pressure to which some part of the Earth's crust is subjected will be accompanied by an increase of temperature. Such an effect would of course provide a neat explanation of the ways in which igneous material moving upwards towards the surface of the Earth remains molten or at least plastic.

How does all this come about? Waldbaum falls back, quite properly, on a discussion of the application to the materials of the Earth's crust of the Joule-Kelvin effect, best known for its importance in refrigeration processes, when cooling is brought about by the adiabatic throttled expansion of a gas. Liquid CO_2 at ambient temperature can, for example, be converted directly to dry ice at -80°C by this means. For every gas, however, there is at a given pressure an inversion temperature above which throttled expansion results in a temperature increase. (The inversion temperature decreases with increasing pressure.) As Waldbaum points out, the extrusion of a solid substance under similar circumstances will result in a rise in its temperature. In physical terms, the work of extrusion is converted into heat either by direct viscous dissipation or by dissipation as kinetic energy. Since the internal energy of a solid is not strongly dependent on pressure, the heat produced during extrusion must raise its temperature.

It is important to know how closely this chain of argument applies to the processes which go on in the Earth's crust. On the face of things, at least, the pressures within the mantle are great enough to satisfy the interests of most thermodynamicists. Given that the so-called adiabatic gradient for the materials of which the Earth's crust is made may amount to as much as 1 K for each kilobar, it is obviously also possible to think of circumstances in

which solid materials are made molten simply by changes of pressure. The chances are, however, that there need to be refinements of the simple picture that suggests itself—the possibility that solids under high pressure at great depths in the crust or mantle could be induced to fly upwards as liquids whenever decreases of pressure took place. Moreover, much depends on whether phenomena such as convection in the mantle, described, for example, by Turcotte and Oxburgh (*J. Geophys. Res.*, **74**, 1458; 1969), can be properly regarded as adiabatic processes. Waldbaum says that even if friction, viscosity and turbulence are ignored in these discussions, the circumstances are such that the ratio $(\partial T/\partial P)_H$ is greater than the ratio $(\partial T/\partial P)_S$, so that the temperature must increase. Where most discussion of Waldbaum's article will be concentrated is on the supposition that these processes are strictly adiabatic or isenthalpic in the sense of the Joule-Kelvin equation.

Only a close definition of what precisely is meant by constant enthalpy—the old-fashioned heat content—is sufficient to resolve the difficulty. Does the definition of the enthalpy of a material include kinetic and gravitational energy, or are these quantities excluded? If the Joule-Kelvin equation should be applied only when changes of gravitational and kinetic energy can either be ignored or compensated for, there is obviously a possibility that the estimates of Joule-Kelvin heating which Waldbaum has made are substantially too great. Obviously it would be valuable to see a closer discussion, along the lines already provided by Mackenzie (*J. Geophys. Res.*, **72**, 6261; 1967) among others of the departures from hydrostatic equilibrium of the pressure differences within convecting regions of the crust and mantle of the Earth. Another difficult, requiring further examination is that there may be many circumstances in which it may be invalid to assume that convection is an adiabatic process. Certainly those parts of the Earth's crust where gravity measurements suggest that convection is rapid are also places at which the heat conduction anomalies are most marked.

For practical purposes, what Waldbaum has predicted is that there will be circumstances in which the process of viscous dissipation within a convecting fluid could result in an increase of temperature in the rising parts of the fluid. This is the hare that thermodynamicists are invited to chase. More immediately, however, it does seem clear that Joule-Kelvin heating of a solid may be important in processes of rapid change as in the impact of meteorites or the effects of seismicity beneath the surface. The process also may be important in the formation and intrusion of kimberlites as well as in violent volcanic eruption. How much more widely applicable may be Joule-Kelvin heating in tectonic processes remains to be seen.

EARTHQUAKES

Control by Explosion

from our Geomagnetism Correspondent

BECAUSE earthquake prediction has proved so intractable a problem, the emphasis within earthquake research has moved strongly towards the possibility of control and modification—a development which was as unexpected as it is exciting. In common with many great scientific discoveries, the idea that major earthquakes might be modified rather than allowed to take their sometimes disastrous course arose “accidentally”, though with human help. From the earthquakes which apparently followed the filling of the Hoover Dam during the late 1930s and the disposal of waste chemical and biological weapon materials into a Denver well during the early 1960s there developed the hope that the controlled injection of fluids into regions of tectonic stress might lead to the more gradual release of strain energy. A second possible control mechanism later became apparent when it became clear—chiefly from activities in Nevada—that underground nuclear explosions often lead to the release of energy not derived directly from the explosions themselves. Each of these examples, however, well illustrates the two-sided nature of the strain release phenomenon. The hope that fluid injection and explosions may one day be used to ensure a gradual strain release must be balanced by the fear that less well-regulated experiments could lead to a man-made disaster.

As far as underground nuclear explosions are concerned the best evidence for the interaction between the explosive source and the surrounding rock is the frequent production of horizontally polarized SH and Love waves. Analysis of the radiation patterns of these waves suggests that relaxation of stress leading to the radiation of strain energy takes place around the explosion cavity. The amount of strain energy released and the radius of the relaxation zone have not yet been determined accurately, although from the explosion studies carried out so far it is clear that the energy released in hard rock can be less than the equivalent seismic energy of the explosion itself. The only known, but important, exception was explosion Hardhat (in granite).

Toksöz and Kehr (Science, 173, 230; 1971) have now taken previous studies further by analysing the surface wave radiation patterns produced by two underground nuclear explosions at the Nevada Test Site, Pile Driver and Greeley, both of which generated Love waves and released considerable strain energy. Pile Driver (58 kton) was detonated in granite and Greeley (825 kton) in zeolitized tuff. Comparison of the results with similar data from other

explosions clearly shows that explosions in harder rock (for example, granite) usually release more tectonic strain energy than explosions in soft media such as tuff, alluvium and salt. In the latter cases low rigidities prevent the accumulation of shear strain energy owing to plastic deformation under stress. This is particularly true of salt in which no Love waves are generated at all.

It does not follow, however, that all explosions in a given medium radiate proportionally the same amount of strain energy. Thus in granite, for example, the ratio of the surface wave energy for strain release to the surface wave energy of the explosion itself in the 15 to 22 s range (E_t/E_e) was 13.65 for Pile Driver, 12.00 for Hardhat and only 1.05 for Shoal (western Nevada). It would seem that the magnitude of the pre-existing tectonic stress in the rock is also important—as might only be expected, the E_t/E_e ratio is greater for greater ambient stresses. But tectonic stress and the particular medium seem to be the only two principal parameters involved. Thus Pile Driver and Hardhat, whose sites were only half a kilometre apart, each released strain energy

proportional to its own explosive energy. Toksöz and Kehr conclude, furthermore, that it is the regional tectonic situation which controls the radiation pattern and that the strain energy release arises from close to the explosion and not from earthquakes triggered 10 or more kilometres away. Adjustments at these distances take place gradually as evidenced by the aftershock activity produced by some large explosions.

As Toksöz and Kehr point out, the fact that Pile Driver, Hardhat and, to a lesser extent, Greeley, had high E_t/E_e ratios means that under certain circumstances explosions may be used to release strain energy far in excess of the energy of the explosion itself. The prospects for earthquake modification through artificial strain release are thus encouraging. And because the strain is released from close to the explosion point it would seem that in a practical situation the point of stress reduction could be defined and controlled quite closely. By the same token, however, it would not be possible to deactivate regional stress fields by a single explosion. Nor is it yet known how long it would take for a distressed area to

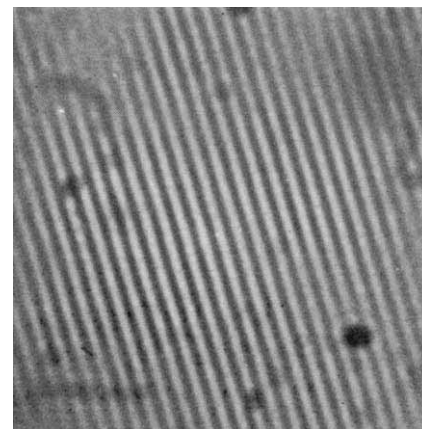
Lasers, Gratings and Microcircuits

IN next Monday's *Nature Physical Science*, Dr V. I. Little and his colleagues at the Royal Holloway College, London, report another elegant method for producing finely ruled gratings with a laser. Their original method made use of the selective etching of gold from a glass substrate at the antinodes of the electric field associated with the standing light wave in a ruby laser cavity, but they have now discovered the opposite effect—that the condensation of gold vapour onto a glass plate can be selectively inhibited with a periodicity characteristic of the laser standing wave.

During a 50 ns giant pulse from a Q-switched laser, gold is evaporated from a film inside the laser cavity and some of the gold atoms approach a glass collector plate placed at an angle to the axis of the laser and about 0.1 mm from the gold film. Provided that the gold reaches the plate before the laser pulse decays, Little *et al.* find that it only deposited at the nodes of the standing wave and that the pattern generated is similar to that produced by the etching method. The next step in the work will be to devise a system for producing these “modulated” films in a more controlled manner using a continuous standing wave from an argon ion laser.

In the longer term all these techniques could have important consequences for the manufacture of

microcircuits and, as well as making modulated gold films, Little's group have been able to deposit dielectric films in a similar way. This opens up the interesting possibility of producing a series of very small capacitors or waveguides, spaced 2.5 μm or so apart, by depositing a dielectric layer between two conducting layers. If the deposition process could be carried out in two laser beams, aligned in such a way that two crossed gratings are formed, then the matrix of rectangular capacitors so produced could be the basis of a cheap and compact electronic memory of storage device.



Microphotograph showing part of the gold pattern.

reaccumulate its original stress. Pile Driver, detonated within half a kilometre of Hardhat but four years later, radiated proportionally the same amount of strain energy as Hardhat. This could mean that the original stress had built up again within four years. The results are inconclusive, however. The yield of Pile Driver was about ten times greater than that of Hardhat and so the volume within which strain was released was correspondingly larger.

But although these results are, in a sense, encouraging, they also have their disturbing aspects. Because the proportional energy release (but not the absolute energy release) is independent of the shot yield, but is instead controlled by the rock properties, a large explosion could release large quantities of tectonic strain energy. A one-megaton explosion with an E_s/E_0 ratio similar to those of Pile Driver and Hardhat, for example, would release energy equivalent to a magnitude 6.3 earthquake. A ten-megaton explosion would, under these circumstances, be equivalent to a magnitude 7.2 earthquake. For explosions of these yields hard rock and high tectonic stress are clearly a hazardous combination.

VISNA VIRUS

Oncogenicity Detected

from our Cell Biology Correspondent

AT the end of last year and early this year four reports appeared stating that reverse transcriptase, capable of using endogenous viral RNA as well as added synthetic RNAs and RNA-DNA hybrids as templates for DNA synthesis, was present in visna virus and simian foamy virus particles. Until then this enzyme activity had, among viruses, only been detected in the virions of the RNA tumour viruses, where its presence could be explained in terms of Temin's provirus hypothesis of transformation by these viruses.

Reverse transcriptase in two viruses which had never previously been suspected of being oncogenic frayed the edges of an otherwise tidy situation; the sweeping generalization that only RNA tumour viruses contain reverse transcriptase, because only they among the RNA viruses need to integrate their genome into that of their hosts, could no longer be made. But was that really the case? Neither visna virus, which causes a slowly progressing neurological disease of sheep, nor simian foamy viruses, which have not been associated with any known monkey disease, had ever been tested for oncogenicity. So Takemoto and Stone set about remedying that; they are now able to report (*J. Virol.*, 7, 770; 1971) that visna virus and an antigenically related virus, progressive pneumonia virus (PPV) of

sheep, which causes a slowly developing pneumonia and also contains reverse transcriptase as Takemoto and Stone have found, are able to transform mouse cells.

Some three to four weeks after infection with either visna or PPV, cultures of mouse cells (line AL/N and Balb/c 3T3) develop foci of spindle shaped cells from which Stone and Takemoto have established stable transformed lines, which grow rapidly, are not subject to contact inhibition and are tumourgenic for susceptible mice. The medium in which these transformants grew lacked detectable virus, but by cocultivating the transformants with

normal sheep testis cells both visna virus and PPV could be rescued; moreover, the rescued virus is identical to virus isolated directly from sheep cells and can be used to transform fresh cultures of murine cells.

To obviate the obvious criticism that some other known oncogenic virus was responsible for the transformation after cells were exposed to these two sheep viruses, Takemoto and Stone tested for antigens of murine sarcoma leukaemia viruses and for T antigens of oncogenic DNA viruses; all the transformed lines gave negative results. Clearly, visna virus and PPV, which have many of the morphological characteristics of RNA

The Mechanism of Phloem Transport

TRANSPORT of sugars in plants, from sites of synthesis or food storage to those of utilization, takes place in the phloem through a system of fine tubes—the sieve tubes—which are interrupted at frequent intervals by a series of perforated baffles, the sieve plates. The mechanism by which large quantities of sugar solution are transported at rates which are sometimes in excess of 100 cm per hour is one of the principal unsolved problems of plant physiology.

More than a century has passed since it was suggested by the German botanist, Hartig, that the motivating force for phloem transport is a hydrostatic pressure gradient developed between the source of carbohydrate and its sink. This "pressure flow" hypothesis satisfactorily accounts for many of the features of phloem transport and is still favoured by most plant physiologists today. It has been calculated that the hydrostatic pressure gradients likely to exist are sufficient to induce flow at the rates observed—at least in plants with wide sieve tubes—as long as the pores in the sieve plates are not obstructed.

Much attention has been paid recently to the state of the pores in functioning sieve tubes, but the evidence from electron microscopic studies is contradictory. Sometimes the pores appear open, and in other cases they are clearly blocked. Much seems to depend on the way the material is prepared for microscopic examination, and to confuse the matter further the same observations are interpreted differently by different investigators. Proponents of the pressure-flow hypothesis contend that the pores are normally open but can readily become blocked during preparation of the tissue. Other investigators maintain that the pores in functioning sieve tubes are filled with fibrous membranous structures which somehow assist in transport and that these materials are sometimes displaced leading to the

appearance of open pores in sections.

In an attempt to resolve this dilemma, Jarvis and Thaine, of the Grassland Research Institute, Hurley, have been experimenting with new methods of preparing phloem for microscopic observation and they report their observations in next Wednesday's *Nature New Biology*. As an alternative to chemical fixation, the tissue is frozen rapidly while still attached to the plant and sectioned in a cryostat for examination in the light microscope. In material prepared in this way strands with a distinct boundary layer enclosing groups of parallel sub-structures were seen in sieve tubes. The diameter of a strand was similar to that of the sieve pores into which some strands appear to pass. These strands are believed to be the "transcellular" strands reported earlier by Thaine and looked on by some other investigators as artefacts.

There has been a suggestion that the Thaine strands are identical to the slime or P-protein fibres which regularly occur in sieve tubes and seem to be involved in blocking sieve pores in response to wounding. Jarvis and Thaine put forward the idea that slime strands may be constituents of the larger transcellular strands which have been partly degraded.

If, as Thaine believes, the transcellular strands are tubular structures passing through the sieve pores, it is likely that they are the conduits in which longitudinal transport of sugar takes place. Thaine has suggested that the solution is propelled through these tubes by rhythmic contraction and relaxation of protein fibres in the walls. A theoretical analysis of such a peristaltic mechanism has recently been made by Ailman and Anderson (*Ann. Bot.*, 35, 761; 1971) and they concluded that the model is a feasible one. The observations of Jarvis and Thaine provide further evidence for the physical reality of transcellular strands on which the hypothesis is based.

tumour viruses and an RNA genome which in size and response to denaturation is remarkably similar to those of the RNA tumour viruses (Lin and Thormar, *J. Virol.*, **7**, 582; 1971), should be grouped with the oncornaviruses. Moreover, Stone and Takemoto's findings, which are fully in keeping with Temin's hypothesis, should spur on the screening of other RNA viruses initially for reverse transcriptase and then oncogenicity if they have the enzyme.

But why do visna virus and PPV contain a reverse transcriptase when they do not apparently cause tumours in their natural host, the sheep? Both are so called slow viruses which chronically infect sheep for many months and even years; both cause very slowly progressing diseases (the parallels with tumour viruses and cancers are obvious enough), and it may well be that the maintenance of slow virus infections depends on the production of a DNA provirus, as does tumour virus infection. As Takemoto and Stone point out, the concept of a DNA provirus should not be overlooked in studies of any slowly progressing disease which has been suspected of having a viral aetiology.

JUPITER

Great Red Spot

from a Correspondent

JUPITER'S Great Red Spot is an unsolved problem of long-standing in astronomy. Nobody to date has produced a satisfactory explanation for the features of this elliptical blemish, although high resolution observations and subtle theorizing are now reducing the number of possibilities.

Observers at the New Mexico State Observatory have photographed Jupiter with a 61-cm telescope on every possible opportunity since 1963, and they can fix the position of the red spot to within 0.2°. A summary of the 1970 observing season prepared by E. J. Reese (*Icarus*, **14**, 343; 1971) gives a good impression of the motions of the surface markings. Last year the red spot was very dark and well defined, and it had mean lateral dimensions of 27,800 km by 13,800 km. There is now considerable information on the detailed motion of the spot, particularly its drift in longitude. In Reese's data the 3-month oscillation discovered five years ago shows up strikingly, with an amplitude of around 1°, and Reese comments that the motion is sufficiently regular for the extreme points of this harmonic motion to be predicted with an uncertainty of only 4 days. Moreover, on longer time scales, the spot probably has a 9-year oscillatory motion, and there is a systematic long term wandering which is aperiodic.

High quality observations such as these are winnowing down the possible models of the red spot, and Carl Sagan, of Cornell University, has recently tackled the problem using propositional calculus (*Comments Astrophys. Space Sci.*, **3**, 65; 1971). His method is to set down a few well established facts with which an acceptable theory must be consistent; these include such properties as the red colouration of the spot, its uniqueness, its periodic longitude excursions and its long term stability. These features are then assembled into a "truth table" or check list for interrogating the theories.

The floating raft hypothesis advanced in 1881 has had a good run; basically it says the red spot is something floating in something else, and is careful not to be too precise. The Jovian raft founders, however, because it cannot really explain the oscillations, and Sagan's table prognosis is decidedly negative. Another class of theories treats the red spot as a meteorological phenomenon. Foremost of these theories is Raymond Hide's Taylor column hypothesis: when a homogeneous fluid flows over an obstacle a relatively stagnant tube of fluid is formed; the red spot is a visible manifestation of a Taylor column caused by a topographical feature on the planet. Sagan's analysis, however, gives this idea a bruising, and he questions how the uniqueness, colour and motion of the red spot can be fitted into such a model.

A novel approach to the problem of

the red spot is advocated by W. B. Street, H. I. Ringermacher and G. Veronis (*Icarus*, **3**, 319; 1971). They fuse the attractive parts of the raft and column hypotheses to produce a Cartesian diver model which gives a good account of the mobility of the red spot. In its simplest form the Cartesian diver is an inverted float, containing a small amount of trapped gas, in a jar of fluid. The diver can be made neutrally buoyant at a fixed level by exerting a pressure on the fluid. The Jovian diver is visualized as a light phase of solid hydrogen floating in a dense hydrogen-helium fluid; it lies at depths of several thousand kilometres, in the megabar pressure regime, and its base is heated by the planetary interior. Consequently the diver rises to a higher level, where the lower pressure causes some of the hydrogen to melt. As the solid erodes the bubble of heat is released, and so the Cartesian diver can descend to a lower level and grow again.

Although the argument put forward by Street *et al.* is highly speculative the physical processes behind it are reasonable and they are consistent with the observed changes in the size and colour of the spot over the past century. The value of the hypothesis comes in considering the oscillations, because the equations of motion for a diver in a rotating ocean suggest that the longitudinal motion of the red spot consists of several oscillatory components of different amplitude and frequency. These predictions are in precise agreement with periods derived by Reese *et al.*

Nitric Acid in the Stratosphere

RECENT developments in infrared and submillimetre techniques have led to the identification of several previously unknown molecules in the Earth's atmosphere and stratosphere. But in order to make quantitative determinations of the concentration and distribution of such species it has also been necessary to undertake new laboratory investigations of the molecular vibrational and rotational spectra. The necessary use of long optical paths in infrared observations carries with it the great advantage over chemical probe techniques that local contamination by the observation system can be minimized. Recently Murcray *et al.* (*J. Opt. Soc. Amer.*, **59**, 1131; 1969) detected nitric acid in the stratosphere by studying the near infrared absorption of solar radiation using a balloon at a height of 30 km. The spectra were recorded near sunset to obtain a long path length through the stratosphere, and the minimum altitude observed was about 20 km.

These authors have suggested that the nitric acid is associated with the ozone layer in the upper atmosphere but it is also important to know whether

nitric acid is a characteristic constituent of the stratosphere or whether it is accumulating because of pollution in the lower atmosphere. New measurements by Drs Harries, Burroughs and Duxbury (National Physical Laboratory and Bristol University) are reported in the forthcoming issue of *Nature Physical Science*, and these confirm that the nitric acid concentration does indeed decrease with decreasing height as does the concentration of ozone. The new observations are of the submillimetre emission spectrum of the stratosphere observed from a Comet aircraft flying along a controlled path at a height of 12.5 km. At this height there are several important advantages in the emission technique compared with the solar radiation method.

The emission spectrum between 18 and 34 cm⁻¹ shows the well known atmospheric emission lines of H₂O, O₂ and O₃ and several unidentified lines. A parallel laboratory study has, however, shown that, although nitric acid has a strong characteristic rotational spectrum in this region, the unidentified lines cannot be attributed to HNO₃.

BARN OWLS

Catching Mice

from our Animal Behaviour Correspondent

BARN owls (*Tyto alba*) can successfully catch mice in total darkness; they rely on the noise the mouse makes as it rustles through leaves to guide them to their prey. R. S. Payne (*J. Exp. Biol.*, 54, 535; 1971) has demonstrated that the owls can do this even in the absence of other clues as to mouse's whereabouts, such as its smell or the heat given off by its body, and his experiments have shown that the owls are remarkably accurate in both the horizontal and vertical localization of a sound source.

He induced owls to fly towards a loudspeaker that was emitting mouse-like rustles and gauged their accuracy by measuring the distance between the centre of the loudspeaker and the centre of the imprint which the owls' talons made on impact with plasticine surrounding the loudspeaker. This method revealed that the owls seemed to need frequencies above 8.5 kHz, because when these frequencies were removed from the sound source, the birds were much less accurate.

Regardless of its position when it first hears a mouse rustle, an owl always turns to face the mouse and then must have one further sound before it can strike successfully. Payne suggests that this is because the owl localizes a complex sound source by trying to make all frequencies as loud as possible in both ears and would then automatically come to face the source of the sound. To investigate this, Payne placed a microphone in the head of a dead owl at the site of the (now removed) eardrum and played sounds of constant intensity and frequency through a loudspeaker, recording the response of the microphone as the position of the loudspeaker was varied. In this way, he was able to construct a map of "iso-intensity" lines for each frequency, showing the position of "highs" (places

from where the sound was loud) and "lows" in the space surrounding the ear. The owl's sensitivity was found to rise sharply to a maximum along the line of sight. A low in one ear always corresponded to a direction of good hearing for the other ear, and this was interpreted as a special adaptation to sound localization, because it would have the effect of sharpening the frontally directed regions of maximum sensitivity.

Comparisons of positions at which regions of maximum and minimum sensitivity for a given frequency occurred in the vertical plane revealed that in the right ear such regions are roughly

10–15 degrees higher than in the left ear, presumably as a result of the marked asymmetry of the external ears. A sound which was loud to the right ear could therefore be soft to the left. If the owl then tilted its head in the vertical plane, the relative loudness of the sound in the two ears would change, and this too seems to be an adaptation to reduce ambiguity about the position of a sound.

One of the most characteristic features of an owl, the heart-shaped face, may also be connected with its hearing ability; it may act as a parabolic reflector to catch sound.

Repairing Mispairing of DNA

IN next Wednesday's *Nature New Biology* a simple observation is described which may have profound genetical implications. Using the multicellular alga, *Ulva mutabilis*, Fjeld has produced evidence which lends support to the master-slave hypothesis of unidirectional correction of mispairing of DNA and also gives an indication of the reasons for only complete mutations being found after ultraviolet irradiation.

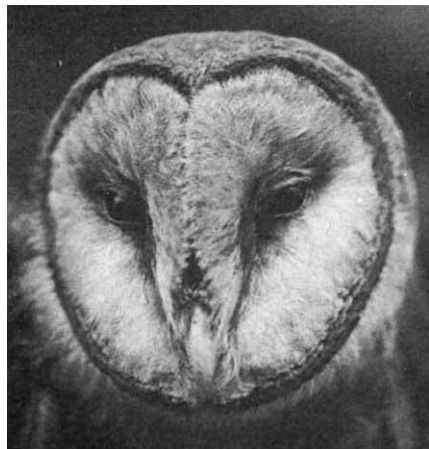
It seems surprising that *Ulva mutabilis* has not been used more frequently for genetic studies because individual cells of this haplo-diplontic alga can be induced to form gametes which will germinate parthenogenetically giving haploid plants. Development starts as a single filament of cells which later becomes tubular, and the characteristic plant form is assumed by elongation of the basal cells to form the stem and the continued division of cells at the apex to form the blade. Chimaeras can be induced by irradiation of young algal germlings and Fjeld has found that there are two kinds which occur in equal numbers; one is genetic so that the gametophytic progeny also show the chimaeric characteristic and the other is merely phenotypic and the gametophytes appear wild type. The chimaeras examined were those with a basal part very like wild type but with a narrow protuberance at the apex which developed into a long ribbon, and those with a bulge somewhere on the blade.

In twenty-six plants with this first type of alteration the apical protuberance did not develop very far, and when the cells of these plants were induced to form gametes the change proved to be merely phenotypic. The apical protuberance on a further twenty-three plants, however, continued development into a long ribbon and analysis of these plants showed that the change in this instance was genetic. Those plants which responded to the ultraviolet light by producing a bulge on the blade also showed the

genetic and phenotypic chimaeras to be produced in equal numbers.

It is easy to understand how the genetic alterations can be induced by ultraviolet light, but the nature of the temporary phenotypic alteration is more puzzling, and Fjeld's suggestion that this lies at the level of the gene is interesting. His explanation centres around the fact that only one strand of the DNA is involved in transcription and a mutational event occurring in this strand would be transcribed into an altered mRNA. This cell and any immediate descendants would thus be channelled into an abnormal developmental path giving rise to the chimaeras. Fjeld then goes on to suggest that if the strand which is being transcribed is corrected, using the other strand as template, a phenocopy appears, for all the gametophytic progeny from these cells, in which the abnormal development has been corrected, will be wild type. Up to this point his explanation means that the ratio of genetic to phenotypic chimaeras would be 2:1, for the probability of mutation and correction would be the same in both strands. Half of the mutations in the transcribed strand will thus revert to wild type and will register as phenotypic chimaeras, although if the same type of event occurs in that DNA strand which is not transcribed the mutational event will be unnoticed. Only mutations in this strand which do not revert and which register as genetic chimaeras will be recorded so that there would be an imbalance in favour of genetic changes.

There are many implausible ways of explaining away the discrepancy, but Fjeld's ideas are quite attractive for he chooses to believe that the transcribed strand is always corrected against the other strand but not vice versa. Mutations in the transcribing strand will thus always give rise to the phenocopies, whereas mutations in the non-transcribing strand will produce the true genetic alterations. The expected ratio will then be 1:1.



Barn owl (photo: Zoological Society of London).

BACTERIA

The Hot Life

from our Microbiology Correspondent

THE biochemistry of microorganisms able to grow at high temperatures has fascinated biologists for a long time, and the discovery that some bacteria can grow in boiling water (T. D. Brock *et al.*, *J. Bact.*, **107**, 303; 1971) is certain to redouble interest in this area of thermobiology. Brock and his colleagues have been studying for several years the microbiology of thermal springs in Yellowstone National Park and their recent work has centred on Boulder Spring which is fed by two superheated sources. An understanding of the bacteriology of the effluent channel is now beginning to emerge, this particular habitat has a temperature of about 91° C which, at the altitude of Yellowstone, means boiling water.

The bacteria which colonize these inhospitable waters are unknown and have not been cultured in the laboratory, but the elegant techniques which Brock has developed for investigations *in situ* have enabled many of the physiological properties of these organisms to be defined. Brock *et al.* have found, for example, that the generation times of the bacteria last for 3 to 7.5 h at temperatures exceeding 90° C. But their latest study reveals the significant fact that these temperatures are only slightly higher than the optimal temperatures for these organisms.

The technique for determining the environmental optima is very simple. Glass cover slips were suspended in the effluent stream until the colonizing bacteria had formed a dense covering and then the incorporation of various labelled organic substrates was followed in tightly closed vials. The amount of isotope uptake paralleled the amount of bacterial biomass but only occurred if sulphide, or some alternative reduced sulphur compound, was present. The optimal effect was produced with a sulphide level of 13 µg per ml., and although this concentration increased the uptake of all compounds tested, the most dramatic stimulation occurred with leucine, acetate and thymidine (Boulder Spring water itself contains about 3 µg sulphide per ml.). Brock *et al.* conclude that these bacteria can utilize sulphides, sulphite and metabisulphite as energy sources and resemble bacteria like *Beggiatoa* which can incorporate organic matter when reduced sulphur is available. The temperature optimum for isotope uptake stimulated by sulphide ranged from 80° to 90° C, irrespective of the organic substrate, and significant incorporation even occurred at the higher temperature of the stream, 91.5° C.

At least two types of Gram negative bacteria were observed to colonize the

cover slips and these could be distinguished by their filamentous or bacillary morphologies. But are the physiological data representative of both bacteria? Autoradiography was unfortunately unable to provide the answer because of the interaction of the sulphide with the photographic emulsion. Although attempts to cultivate these organisms have failed so far, success in this endeavour will be essential to elucidate their peculiar capacity of being able to adapt to boiling water.

ICHTHYOLOGY

Red Sea Migrants

from our Marine Vertebrate Correspondent

ALTHOUGH the Suez Canal is blocked to shipping it is still open as a passageway for fish. Two more Red Sea fishes have been discovered recently on the Israeli Mediterranean coast (A. Lourie and A. Ben-Tuvia, *Israel J. Zool.*, **19**, 203; 1970). One of them, *Pelates quadrilineatus*, is a small, longitudinally striped fish which is found in the coastal waters of the Indo-Pacific region from southern Africa to Australia. It has long been known from the Red Sea but no reports of its occurrence in the Suez Canal are known. This contrasts with

the history of the second species, *Crenidens crenidens*, a sea bream which is common in the Red Sea and was reported as early as 1902, within 30 years of the cutting of the canal, as one of the most common fishes in the canal and in the Bitter Lakes, and had reached as far as Port Said. Lourie and Ben-Tuvia, who work at the Sea Fisheries Research Station, Haifa, collected in February 1970 many specimens of *C. crenidens*, up to 15 cm in body length, in a shallow hypersaline lagoon on the northern coast of Sinai.

Other Red Sea immigrants to the Mediterranean have not proved to have such limited habitats and several of the species are common enough to appear regularly in the commercial fish catches of Israel, the Lebanon and Egypt. According to a recent check list of the Mediterranean fishes of Israel (*Israel J. Zool.*, **20**, 1; 1971) by Ben-Tuvia, as many as thirty of the 284 species are immigrants from the Red Sea. The fish fauna of the eastern basin totals only a little more than half of the total of 540 Mediterranean species known, and although this is partly the result of the comparative sparsity of field work and study of critical areas, it is clear that it is a relatively impoverished fauna. Fishes of Red Sea origin have perhaps gained a place in the eastern basin more

RNA.DNA Complexes and Antibody Production

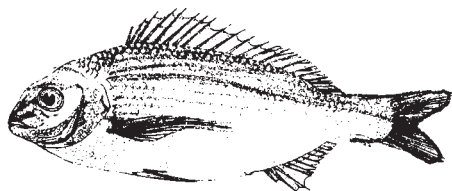
SYNTHETIC hybrid nucleic acids containing DNA and RNA chains are familiar tools of biochemists investigating the properties of various nucleic acid polymerases, and measuring the extent to which natural RNAs hybridize with DNA is a technique widely used by molecular biologists probing gene expression in one cell system or another. But complexes between RNA and DNA which occur naturally in cells have seldom been identified, and for that reason alone the experiments reported by Koros, Koster and Mowery in next Wednesday's *Nature New Biology* will attract considerable interest.

Koros and his colleagues have been investigating the spleen cells of mice, immunized with sheep erythrocytes, which are capable of producing IgM antibodies against sheep red cells and can be assayed *in vitro* by their ability to lyse these erythrocytes. Using an autoradiographic technique they have followed the incorporation by these cells of pulses of ³H-thymidine or ³H-5-uridine. As anticipated, the thymidine label is incorporated into material which can be completely digested by deoxyribonuclease and is therefore almost certainly DNA.

The uridine incorporated by these antibody forming cells, by contrast, re-

sponds to digestion by deoxy and ribonucleases in an unusual way. Little if any of the label is removed from the cells by deoxyribonuclease which indicates that little of the uridine can have been converted by the cells to the DNA precursor deoxycytidine. But only about half of the incorporated uridine is digested by ribonuclease, and half the label survives this procedure. If, however, the cells are first digested with deoxyribonuclease and then with ribonuclease all the labelled uridine is digested.

Koros *et al.* believe that these results indicate that in antibody forming spleen cells much of the RNA which is being made remains somehow complexed with DNA and is thereby protected from ribonuclease digestion until, of course, the DNA is digested. Furthermore, they report that spleen cells which are not making antibody incorporate uridine into RNA, 98 per cent of which can be digested by ribonuclease alone. This result, they claim, shows that RNA.DNA complexes are far more abundant in cells making antibody than in similar cells which have not been stimulated to antibody production. As they point out, these DNA.RNA complexes may be involved in antibody synthesis, acting perhaps as messengers, and they are now trying to test this fascinating idea.

*Crenidens crenidens.*

easily on account of this relative poverty of the native fauna, there being more unfilled ecological niches than there would be in the western basin. Their spread within the present century has, however, been rapid and at least sixteen species must now be regarded as common, some even as far afield as the coasts of Cyprus and Anatolia.

Very little seems to be known about the effects of this influx of Red Sea forms on the native fish fauna. As Ben-Tuvia observes, these fish, and especially the common ones, must be important in food chains and the general biological balance in the area. It may be significant that better than average catches of the immigrant lizard-fish, *Saurida undosquamis*, coincide with years when the native Atlanto-Mediterranean hake, *Merluccius merluccius*, is scarcer than usual. The connexion may not be direct, for *Saurida* and the Red Sea red mullet, *Upeneus moluccensis*, are noticeably more abundant in years of above average temperatures than in cool years in Israeli waters.

It is clear, however, that although this form of biological pollution of the eastern Mediterranean has reached considerable proportions, it is still continuing. With the drastic control exerted by the Aswan dam on the freshwater inflow of the Nile to the Mediterranean further changes in the marine fauna of this area could well take place.

TOXINS

The Perfect Poison

from our Molecular Biology Correspondent

VENOMS, it seems, are frequently more effective than their separated toxins. The ingenious rattlesnake for example, as Hendon and Fraenkel-Conrat (*Proc. US Nat. Acad. Sci.*, **68**, 1560; 1971) now show, secretes a pair of proteins, which act concertedly, one evidently softening up the victim for the other. Crotoxin, as isolated, behaves as a single component in the usual fractionation systems. When, however, amino-groups are chemically modified, an insoluble fraction appears, which is a basic protein, separated from its acidic partner. In ion-exchange chromatography crotoxin separates into two peaks, which, however, seem functionally identical. A tryptic digest of the material from these peaks shows only small differences, sug-

gesting that at least one of the two proteins is heterogeneous, but the acidic and basic components have not separated. In 6 M urea, however, the results are very different, two protein peaks appear of very different amino-acid compositions—one acidic and one basic—eluting at widely different positions. The molecular weights, by detergent gel electrophoresis, are about 8,400 and 13,000.

The acidic protein is not neurotoxic, and does not cause haemolysis, though it is able to cleave lecithin. The basic protein, on the other hand, carries all the haemolytic activity of the venom. Between them the two proteins manifest ferocious neurotoxicity. As Hendon and Fraenkel-Conrat note, enzyme systems that function only when two components are both present are by no means unknown, one subunit species in an oligomer directing the specificity of the other. Alternatively it might be conjectured that lysis of a membrane is necessary before the neurotoxin can go to work.

A rather similar situation has been uncovered by Lowy, Sarmiento and Mitchell (*Arch. Biochem.*, **145**, 338; 1971) in a study of bee venom. This

contains a variety of proteinaceous materials, including a hyaluronidase, a phospholipase, and several physiologically active peptides. This package turns out to be lethal to larvae. Lowy *et al.* have purified two peptides—melittin, which is well characterized and has been sequenced, and is the principal component of the venom and one other—and have examined their effects on *Drosophila* larvae. The new peptide is called minimine, for its physiological effect is nothing less than to minimize the insect. Its molecular weight is some 6,000 and it contains cysteine, or cystine. In appropriate doses it does not kill the larvae, but induces a condition of lethargy, in which the effort of feeding seems to be beyond the creature's will-power.

In a second article, Mitchell *et al.* (*ibid.*, 344) report the effects of melittin, which is an oligopeptide of twenty-six residues (molecular weight, 2,800). It is known to possess haemolytic activity, and it now seems that it is also a neurotoxin for the larvae. It is a non-competitive inhibitor of acetylcholinesterase, antagonized by cations—the first case, apparently, of such an effect by a polypeptide.

Cooperation Between Hapten and Carrier *in vitro*

IN recent months, cellular immunologists have been turning their attention to the hapten-carrier. Some of the questions being asked are do B (bone marrow derived) cells and T (thymus derived) cells respond to hapten and carrier respectively, are they specific in their responses, and what are the receptors on the responding cell populations?

An ingenious combination of techniques using *in vivo* and *in vitro* systems has been adopted by Christina Cheers and her colleagues to investigate these problems and they report their results in next Wednesday's *Nature New Biology*. 3,5-Dinitro, 4-hydroxyphenylacetic acid (NNP) was coupled to fowl gammaglobulins (or ovalbumin as a carrier specificity control), and the hapten protein conjugate thus formed was injected into mice, of which the spleens were later harvested. Primed spleen cells in culture in the presence of antigen were shown to be antibody producing by a plaque assay technique using sheep erythrocytes coupled to NNP as target cells for lytic antibody.

In the initial experiments the carrier used for priming *in vivo* and recall *in vitro* was varied, and it was shown that homologous carrier was required to obtain a satisfactory recall response. On the other hand, if cells primed to heterologous carrier were added to cultures in which recall was being attempted by the use of a heterologous

carrier-hapten antigen, significant enhancement of the anti-hapten antibody was observed. If either the carrier primed cells or the hapten primed cells were incubated with an anti-immunoglobulin serum there was a marked inhibition of the immune response. The inference here is that both the carrier and hapten primed cells have immunoglobulin-like receptors for the antigens to which they are primed. When combinations of parental and F₁ cells were used in conjunction with specific anti-allosera it was possible to show that the antibody was derived chiefly from the hapten primed cells.

In a further series of experiments Cheers *et al.* injected thymocytes and antigen into irradiated mice. The primed thymocytes were harvested from these animals and were shown effectively to substitute for carrier primed whole spleen cells in enhancing the anti-hapten response of cells primed to a heterologous NNP-protein conjugate.

This whole series of experiments tends to confirm and extend the results of, among others, Raff (*Nature* **226**, 1257; 1970) and his colleagues. There is little doubt that in the fullness of time studies *in vitro* of immune responses in association with the use of cell populations of defined anatomic origins will greatly assist understanding of the nature of immunological responsiveness.

SEAFLOOR SPREADING

Direct Measurement

from our Geomagnetism Correspondent

ON the face of it the direct measurement of the rate of seafloor spreading is an unlikely activity bearing in mind that most of the spreading material is inaccessible, that spreading rates are low and thus that on the oceanic scale the absolute distance of spreading is small even within the human life span. But because of its position astride the mid-Atlantic Ridge Iceland offers a unique opportunity for the direct determination of spreading rate—or at least something closely akin to it—when combined with modern methods of distance measurement. Decker *et al.* (*Science*, **173**, 530; 1971) have now reported the results of just such an experiment to measure the extent of rifting between 1967 and 1970 within the rift zones of Iceland.

During 1967 fifty-eight survey lines, making up a total distance of about 157 km, were measured with a geodimeter. Most of these lines were joined to form two profiles, one across the eastern rift zone and one across the Thingvellir zone, although two, used as calibration lines, lay outside the rift zones in an aseismic area of Tertiary volcanics near the west coast. Seventeen of the survey lines were then remeasured in 1970. A different geodimeter was used here; but systematic errors between the two instruments were resolved by reference to the calibration lines. All of the remeasured lines had apparently increased in length between 1967 and 1970 by distances ranging from 6 to 45 mm. After taking account of an 18 millimetre cross-instrumental difference the lines were found to have lengthened on average by (20 ± 2) millimetres where the quoted error is the standard error of the mean.

The problem with this sort of thing is, of course, that, notwithstanding the sophistication of modern equipment, errors are likely to be large and not easily assessed; and random errors are likely to be particularly troublesome. So how much of the apparent lengthening is random error and how much represents a real extension of the rift zone? Random errors of measurement for eighty repeated observations made in 1967 and for forty-five repeated observations made in 1970 have a normal distribution with a standard deviation of 5.7 mm. Previous experience in California and Hawaii shows such a standard deviation to be reasonable for lines 2 km long; and this is, of course, much less than the 20 mm average lengthening observed. Moreover, various statistical tests carried out by Decker *et al.* indicated extremely low probabilities for the pattern of extensions from line to line within the profiles to have arisen by chance. Accord-

ingly, the net apparent extension of the eastern rift zone profile between 1967 and 1970 was calculated to be (65 ± 31) millimetres, or about 2 cm a year on average. By contrast, the Thingvellir lines showed an average contraction of 2 mm but this was well within the expected errors of measurement.

Is it possible to use this data to determine the nature of rifting in Iceland? Einarsson (*J. Geophys. Res.*, **73**, 7561; 1968) noted the en echelon pattern of rift fractures and related it to shear motions paralleling the rift zones; and in one sense the new data could be taken to support this view. In the eastern rift profile the first three and last lines indicated a net contraction whereas the middle seven gave a net extension (giving an overall net extension). This situation could arise from left-lateral shear movements; but Einarsson had already concluded (*Soc. Sci. Isl.*, **38**, 128; 1967) that the en echelon pattern of fractures near Hekla was caused by right-lateral shear. Einarsson's interpretation and the Decker data are thus inconsistent; and this has led Decker and his colleagues to support the alternative interpretation of Icelandic rifting put forward by Bödvarsson and Walker (*Geophys. J.*, **8**, 285; 1964) in which the rifts are related to crustal extension perpendicular to the strike of the fractures. In this case the measured extension of the eastern rift zone is explicable without complication.

BIOLOGICAL MATERIALS

Standardized Standards

PREPARATIONS of a variety of biological materials are now available free of charge from the National Institute of Medical Research in London, for use as standards to define units of activity or as reference materials. The substances, which are not for human consumption, include angiotensin, anti-

lymphocyte serum and interferon, and are available to scientists in any country.

Unambiguous standard units, which define the biological activity of a compound, have been adopted internationally to ensure that experimental results can be meaningfully communicated among research groups throughout the world. Many units can be defined on paper; for example, enzymatic activity is expressed as the amount of reaction product formed in unit time in precisely described physical and chemical conditions. The activities of other substances, however, cannot be completely characterized by physical and chemical means.

This problem has been overcome by the Expert Committee on Biological Standardization of the World Health Organization, which has established reference preparations for substances used in the prophylaxis, diagnosis and treatment of human and animal diseases, so that their potency can be expressed in uniform terms throughout the world. These preparations are distributed free of charge by the World Health Organization to member countries, and scientists may receive them on request. Further information about this service can be obtained from the WHO International Laboratory for Biological Standards, NIMR, Mill Hill, London NW7 1AA. NIMR also has limited quantities of hormones and antisera, for use in immunoassays, which are available only to people working in the United Kingdom.

These biological standards are intended for calibration, by comparative assay, of the potency of existing national and laboratory standards and are not intended for administration to humans or for general experimental purposes. The list of substances available in reference ampoules ranges widely from pituitary hormones to insulin and immunoglobulins.

Microwave Molecular Line Astronomy

IN next Monday's *Nature Physical Science*, David Buhl and Lewis Snyder describe the techniques and antennae used by the NRAO's group at Green Bank, West Virginia in the study of molecular lines originating in interstellar space at millimetre and centimetre wavelengths. The interstellar environment provides a unique set of "laboratory" conditions with very low temperatures and densities in clouds travelling at high velocity and occupying regions several light years across so that these observations are of interest to chemists and physicists as well as astronomers.

Tiny dust particles in the gas clouds provide surfaces on which chemical re-

actions can take place, and the discovery so far of twenty-one molecules in space has been a great stimulus to the development of radio astronomy in recent years.

The most exciting aspect of this work has been the discovery of many organic molecules, including those of formaldehyde, hydrogen cyanide and cyanoacetylene, which are of great biological significance. Now the field has developed to such an extent that increased sensitivity from improved instrumentation seems likely to provide the means for the detection of weaker lines and for the resolution of known clouds at frequencies corresponding to the stronger known lines to an accuracy of better than one arc minute.

NRDC and the Environment for Innovation

G. E. HAIGH, A. W. PEARSON & D. S. WATKINS

R & D Research Unit, Manchester Business School

M. GIBBONS

Department of Liberal Studies in Science, University of Manchester

This article describes the historical development in Britain of the National Research Development Corporation, the evolution of its policy and the environment in which it now operates.

IN recent years the execution of public policy towards science and technology has been increasingly scrutinized by many, including Parliament. The Parliamentary Select Committee on Science and Technology, for example, recently examined the exploitation of Britain's carbon fibre technology¹, and earlier this year the Secretary of State for Trade and Industry, Mr John Davies, announced that "Mr Docksey, formerly general manager of the Research and Technology Development Department of BP Limited, has agreed to advise me on the arrangements for the exploitation of inventions resulting from public research and the support by the National Research Development Corporation (NRDC) for the development and exploitation of inventions from other sources"².

One of the more important changes in the external environment of the NRDC was the outcome of the general election in 1970. The present British Government takes a far less interventionist view of its role than did its predecessor and this has engendered a determination to hive off some of the more commercially oriented activities which government has accumulated over the years. For example, when British Nuclear Fuels Limited was established recently as a wholly owned subsidiary of the UK Atomic Energy Authority (UKAEA), the government stated its intention that at some future date private enterprise would be invited to participate in the equity of the new company³.

This disengagement has also been demonstrated by government policy on the services to industry which it provides, particularly those of the type previously the responsibility of the Ministry of Technology. Thus the white paper on the reorganization of central government stated of Mintech's successor, the Department of Trade and Industry (DTI): "It will be a major function of the new department, for which special machinery is provided, to review the size and methods of the various services now provided to help industry, in order to determine whether they are a proper charge on the State and, if so, whether the present system of organization is cost-effective and likely to produce the required results or whether other forms of organization would carry out these functions more effectively. These services include . . . government encouragement of industrial research"⁴. One outcome of this new philosophy might be the hiving off of NRDC, which has been functioning during its two decades or so of existence by means of a loan from what is now the DTI, its operating deficit being financed

from the public purse. Such a procedure would of necessity entail alteration of the statutes under which the organization now operates. In particular, a way of accommodating (or dispensing with) NRDC's present obligation to act in the national interest would have to be devised; even within organizations which are wholly publicly owned, the problem of catering for the national interest in bodies which are expected to cover their costs on a relatively short term basis is well recognized. Thus the green paper published by the last Labour administration setting out proposals for a British Research and Development Corporation (BRDC) stated "in the civil R & D establishments, despite a rising demand for their services . . . a considerable and deliberate effort has been made to redirect programmes of work towards problems of immediate concern to industry, and likely therefore to bring early benefits to the economy of the country"⁵. Any definition of national interest of course depends on an accurate forecast of the future social and economic needs of the community, one of the problems which the Programmes Analysis Unit (PAU), established at Harwell in 1967, was designed to consider. The proposed BRDC would have brought together the civil research and development laboratories of the UKAEA and those of the then Ministry of Technology under a single management, with the intention that the organization should undertake work for both government and industry on a contract basis. NRDC would have been "assimilated into this new organization so that its expertise in the exploitation of invention would be brought to bear directly on the new corporation's work". (Fears were expressed at the time that this loss of independence might cause NRDC to become little more than a sales organ of BRDC. With the change of government, the BRDC proposals themselves may be deemed to have lapsed, although many of the issues raised in the debate on the green paper are germane to the discussion of any potential alternative organizational forms for government research which the present administration might propose.) Although NRDC's value seems to have been well recognized, however, the area of expertise was not that which had been foreseen when the organization was set up. It is therefore interesting to note the way in which this apparent dichotomy has arisen as a result of changes in both the environment for innovation and the responses of successive governments to meet them⁶.

Origins of NRDC

The Second World War ended in an air of general optimism about the possibilities of scientific research and technological development. Nevertheless there was great concern in the United Kingdom that this force for potential good be effectively harnessed in the nation's interest. This concern was focused on four problem areas.

Since the adoption of the Haldane principle of independent research facilities, the government had been responsible for by far the greater part of research expenditure in the United

Kingdom, most of this research being undertaken in the government's own research establishments or in universities. Concentration of effort on specific objectives during the Second World War had accelerated the application of scientific and technological knowledge, techniques and inventions; the peacetime problem was to harness these same activities to industrial needs. Although the Department of Scientific and Industrial Research and the associated government-aided, autonomous industrial research associations (RAs) were active in the application of research to commercial ends, there was no obvious way in which economically valuable research results arising from government-funded research in other institutions could be exploited. Thus a Nuffield College report⁷ recognized that "when universities become possessed of knowledge of high commercial value, there is a need for them to secure utilization of such discoveries in the interests of economic progress and the public", whereas there was a tacit acceptance of the fact that universities themselves were both unwilling and incapable of successfully commercializing the results of their research. It seemed obvious that some new form of institution was necessary.

A second area of discontent concerned the operation of the patent system. "From the 1930s there had been a feeling among left wing scientists that private inventions were suppressed by corporate business and finance, and that many inventors would come forward if funds were available to them"⁸. The same Nuffield College report had also expressed the view that the patent system could be used to check invention and exploitation rather than to stimulate it. The Swan Committee Report⁹ of 1947 found "no satisfactory evidence of particular examples", but, perhaps influenced by the romantic image of the lone inventor then widely accepted, was "of the opinion that future legislation should be aimed not only at the prevention of 'abuse of monopoly' but also at ensuring the fullest practicable use of the rights conferred by patents towards the development of British production and trade".

The other two areas of discontent were more subjective and chauvinistic. One was voiced by Herbert Morrison in 1944 when he said that "(in the field of scientific research) there is an impression, not without some evidence to support it, that in America and Russia things are happening which we shall do well to emulate. It is generally believed that, in the field of what is called 'fundamental research', British science has as fine a record as that of any country in the world . . . but there is some uneasiness about the application of science to current problems of many kinds, including notably problems of technological development in industry"¹⁰. This feeling that Britain was good at invention but poor at exploitation was compounded by the case of penicillin, which was seen at this time by some as an example of the exploitation of a fundamental British discovery by foreign competition. Any discussion of the reasons for this foreign application of British inventions leads to an examination of the problems of development and the factors influencing innovation in general; this in fact constituted the fourth principal area of discussion.

Central to the problem was the view that innovation or the commercial application of research results could be modelled as a straightforward linear chain, commencing with the "flowering of the tree of human knowledge"¹¹. Although the existence of feedback and the problems of attitude, market needs and so on were noted in passing when delineating this innovation chain through research, development, production and application, the chief preoccupation and concern were with the first stages of research and development. The general acceptance of a simplistic model may have engendered the belief that the efficacy of these various stages could be considered in isolation.

These then were the seminal influences leading the government to announce in 1944 that it was to examine "the need for the establishment of a fund to meet the cost of developing new inventions and of providing facilities for testing new ideas for industry" and how best to integrate this with the existing work of cooperative research associations¹².

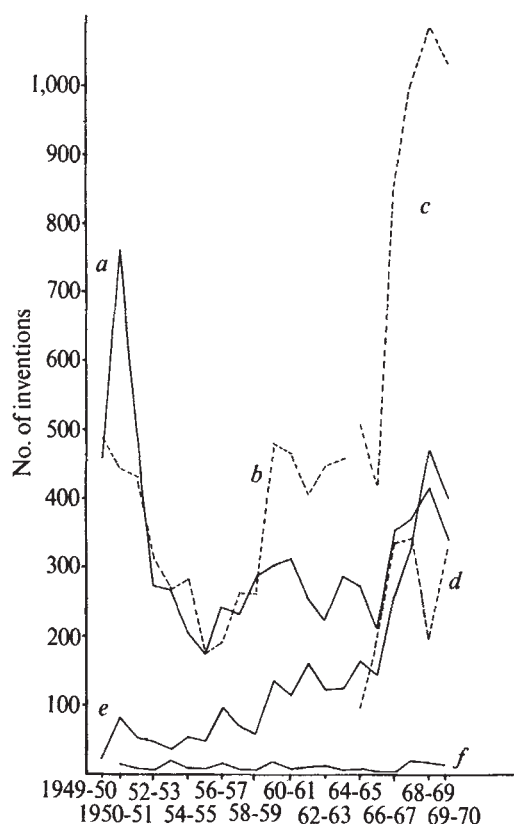


Fig. 1 Number of inventions communicated to NRDC each year (from annual reports). *a*, Research councils and government departments; *b*, total British companies and individuals; *c*, private individuals; *d*, private companies; *e*, universities; *f*, industrial research associations.

Creation of the Corporation

Introducing the Development of Inventions Bill in 1948, the then President of the Board of Trade, Mr Harold Wilson, claimed that the creation of the NRDC "filled an important gap in our scientific and economic life"¹³. The resulting act charged NRDC with (a) securing, where the public interest so requires, the development or exploitation of inventions resulting from public research and of any other invention as to which it appears to the corporation that it is not being developed or exploited or sufficiently developed or exploited; (b) acquiring, holding, disposing of and granting rights (whether gratuitously or for consideration) in connexion with inventions resulting from public research and, where the public interest so requires, in connexion with inventions resulting from other sources¹⁴.

The NRDC was to operate with an initial loan of £5 million for five years; by securing levies on sales in its exploitation activities, it was hoped that the corporation would eventually be able to balance its accounts by taking one year with another. Its aim was to be commercially minded while endeavouring at all times to consider the national interest. During these early years, the emphasis was primarily on the organization's role as an agency concerned with the exploitation of publicly funded research. Consequently NRDC was anxious to establish good liaison with government departments, bodies such as the Medical and Agricultural Research Councils, the universities, and the RAs¹⁵. The universities and RAs were expected to be fruitful sources of the type of developments which NRDC had been set up to exploit; thus much effort was spent establishing good working relationships with these groups¹⁶.

During its early years of existence, the corporation received large numbers of submissions from private individuals, but its "first five years of experience has failed to confirm that a multiplicity of meritorious private inventors stand in need of public assistance. Overoptimistic hopes of the possibilities of effecting

a spectacular increase in the national wealth by supporting them have accordingly been disappointed"¹⁷ (see Table 1).

At this time, NRDC already covered a very wide range of activities from its nurturing of the British computer industry to the development of a potato harvester. Although its continuing concern was with the commercial problems of development and the exploitation and licensing of inventions, it was increasingly recognized that much of the corporation's investment was of a long term nature and, furthermore, was not clearly identifiable with either development or research. Thus in 1954, when the Development of Inventions Act was extended for a further five years, NRDC's research function was clarified, thereby enabling it to support research likely to lead to invention¹⁸.

Table 1 Inventions Considered by NRDC up to 1954

Source of inventions	Total No. of inventions submitted (up to 1954)	Total No. of patent rights assigned for development/exploitation (up to 1954)
Research councils and government departments	2,254	1,322 *
Nationalized industries	5	0
Industrial research associations	45	39
Universities	240	89
Private firms and individuals	1,942	20

* This high take-up rate is chiefly due to the statutory transfer of rights accumulated in previous years.

Industrial Involvement

When the Development of Inventions Act was reviewed in 1958, NRDC's loan ceiling was raised from £5 million to £10 million, and the duration of this advance was extended from ten years to twenty years¹⁹. By 1960, the corporation's licence income more than covered its administrative expenses, but this was still not sufficient to finance all the development projects which it wished to fund without recourse to this Board of Trade loan. The licence income derived from only 3% of the inventions communicated to the corporation and 9% of the patent rights assigned by the corporation for exploitation²⁰.

As traditional sources of capital seemed to be reluctant to invest in innovation at the development stage, NRDC felt that it could benefit the nation by encouraging joint development projects with industry.

By 1964, the managing director of NRDC, then Mr John Duckworth, could state that "our experience is that there are good ideas latent in industry which can be brought forward to the stage of cooperative development after a great deal of joint investigation and planning. . . . The projects only materialize when joint investigations are made in the new climate induced by the realization that the risk of financing development work can be shared. Therefore we need a lot of hard work in close cooperation with industry to bring forward projects worthy of support. The 'conventional' development contract approach for projects chosen by government bodies is most unlikely to lead to profitable enterprises, but contracts based on risk sharing with industry on projects selected jointly with industry can have a significant future"²¹.

More than one third of NRDC's new projects in 1964 were joint ventures and these covered a very wide field, including automatic foundry equipment, diesel engines and fish finders.

At that time it was felt that NRDC had been most useful "in cases where the fruits of invention had been rather long term, or rather indirect, and therefore not of particular commercial

concern"^{22,23}, so an increase in the corporation's joint development activities with industry was deemed a desirable objective. These factors were borne in mind when the review of NRDC's activities leading to the 1965 Development of Inventions Act was carried out²³.

Stimulating Innovation

The 1965 act was the culmination of a debate about ways in which the corporation's contribution as a stimulus to technological innovation in industry could be increased. In essence, the proposals on which the act was based were those made by the President of the Board of Trade in the former administration, Mr Edward Heath, in 1964. Among other things, the act provided that the limit on the loan to NRDC be increased to £25 million, removed the time limit within which advances to it may be made and decreed that government departments should repay expenditure and/or losses incurred on projects carried out on their behalf by the corporation. It also made changes in NRDC's accountability procedures by empowering the responsible minister to give relief in respect of eight years interest on any advance made to the corporation and permitting him, with Treasury approval, to remit its liability to repay loans corresponding to projects written off by the corporation²⁴.

The incoming Labour government's proposed drive to modernize British industry was to be spearheaded by greater use of institutions such as NRDC and the RAs and the use of devices such as civil development contracts²⁵. This approach was perhaps epitomized by the creation of the Ministry of Technology.

The NRDC, its resources expanded by the 1965 act, reorganized in the belief that "the main part of the corporation's business will continue to be concerned with the support of technological development, but that this will increase markedly and will be more broadly based"²⁶. Responsibility for NRDC was transferred from the Board of Trade to the Ministry of Technology, but its operational independence was maintained.

As NRDC's outgoings increased, in large measure through more joint development activities and projects involving increased levels of expenditure, and as its forward commitments became larger, its loan ceiling was soon approached. Increasing exploitation receipts again failed to keep pace with this higher level of activity and NRDC's loan ceiling has since been increased to £50 million.

It would seem, however, that NRDC's own experience after more than twenty-one years and more than 23,000 submissions tends to support the view that "the main reason for the modest scale of NRDC's activities seems simply to be that there are very few inventions worth carrying through the development stage which are not carried through for the want of money"²⁷.

Changing Environment

—It has already been pointed out that NRDC was formed as a result of the complex interaction of several stimuli, among which the following may be singled out.

—There was no agency to exploit developments resulting from publicly funded research.

—There was a general lack of finance for development activities.

—British research results were being exploited abroad.

—It was felt that the patent system might not be encouraging exploitations of inventions originating with lone individuals in particular.

At the time of NRDC's creation, it was felt that, for some reason, foreigners were often more adept at exploiting the results of British inventiveness than the British themselves. Subsequent studies have shown that the availability of development funds is not of itself sufficient to ensure successful innovation; above all, a clearly identifiable market is essential. Thus in the case of penicillin, which was widely discussed when NRDC was set up, the resources to develop and produce the

drug on a large scale were made available only as a result of the intensely felt need for the drug during wartime. It has also been appreciated in recent years that licensing British ideas abroad may itself have an appreciable impact on the balance of trade²⁸. To cite one well known example, Pilkingtons now receive as great an income from royalties on the float glass process as from the production of glass itself using this process²⁹. In fact NRDC has often been criticized for failing to pursue a more vigorous licensing policy abroad³⁰.

An important source of the ideas exploited by foreign competitors was believed to be the lone inventor who, it was thought, had no access to sources of development capital and was not well placed to take full advantage of the benefits of the patent system. The NRDC itself recognized at a comparatively early stage that the number of commercially viable ideas being put forward by lone inventors was negligible. Although NRDC is largely associated in the public mind with the exploitation of an invention from a private individual—namely, the hovercraft—both this and the Bacon fuel cell (similarly acclaimed as a great technological achievement) have so far been important net drains on the corporation's resources, chiefly because there does not seem to be a significant market for either invention in this country at the present time.

It was not the lone inventor, but publicly funded research, which was regarded as its principal source of developments when NRDC was created. Although these have been numerically the most significant source, the corporation could recently report, with the benefit of hindsight, that "the inventions acquired from government establishments and other parts of the public sector did not provide significant revenue, and only the emergence of cephalosporin from Oxford University as an important revenue earner in recent years changed this situation"³¹. Cephalosporin has proved to be NRDC's most significant revenue earner by far.

Computer Software

It should not necessarily be assumed from this that little exploitable research is carried out in government and university laboratories³²; nor does this mean that all such research is exploitable through patent and licensing arrangements. The most obvious example of the last of these types of activity is the development of computer software (which is not patentable) and research in fields such as operations analysis which may not give rise to a definite product. Even in areas where the results are patentable, it does not follow that a separate agency is required to exploit them.

Thus the best way to utilize an area of research expertise (with or without associated patents) may be to create a new organization within the university or government establishment for the specific purpose of exploiting that expertise commercially. Examples of exploitation in this broader sense are the rapid growth in the contract research activities undertaken by government establishments³³, the creation of university-owned companies such as Loughborough Consultants³⁴ and SWIRL (at Bath University) and the formation of spin-off companies such as Oxford Instruments Ltd and Optel Instruments Ltd by people attempting to exploit their university research expertise directly. Even when it is possible to embody research results in the form of a patent, it could be argued that exploitation activities should be carried out at the level of the innovating institution as is done, for example, by certain of the larger universities or groups of universities in the United States. The cutback in the quantity of real resources available for research may mean that universities and government laboratories will increasingly have to seek this kind of extra income to set against their overheads or subsidize their traditional research activities. And the position of a "middleman" in such situations has recently been the subject of extensive debate following the comments of the Select Committee about NRDC's role in the exploitation of carbon fibres¹, although it could be argued that such a middleman is more

insulated from political pressures, as well as being a source of advice.

Two areas in which NRDC has interests at present were not envisaged as its specific concern when it was set up; these are the support of research likely to lead to invention and the support of development within industry—joint development ventures—which have become increasingly important since the 1965 Development of Inventions Act.

In both these areas NRDC was a pioneer and has undoubtedly fulfilled a useful role. But other institutions now exist specifically to fulfil these two functions. The Science Research Council (SRC) recently noted that its objective was to create scientific and technological assets through the support of "research whose timeliness and promise are likely to lead to the discovery of new knowledge and techniques of significant scientific, economic or social benefit"³⁵. The SRC recently set up a separate engineering board so that "added point and impetus could be given . . . to encourage . . . the application of high standards of intellectual discipline not only to the furtherance of knowledge, but to its creative development in the best interests of society at large"³⁶.

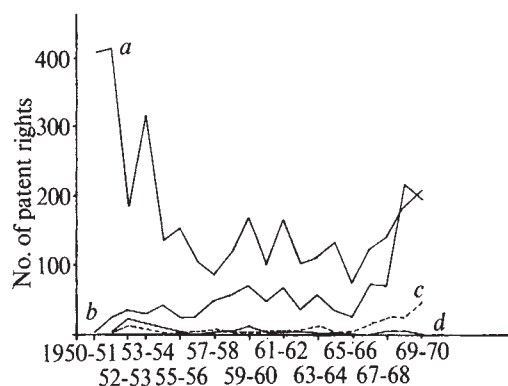


Fig. 2 Patent rights assigned to the corporation each year for further development and/or exploitation. *a*, Research councils and government departments; *b*, universities; *c*, British companies and individuals; *d*, industrial research associations.

As well as providing funds for research likely to lead to commercial exploitation, NRDC has also found it advantageous to participate in the finance of developments in private industry; when the corporation was set up, the possibility that industry itself would be an important source of undeveloped or unexploited new inventions or processes was not then contemplated³⁷. This involvement has taken two forms, participation in the "equity in a development" and participation in the equity of the innovating company itself.

In the former case involving a company which is presumably trading profitably, NRDC has been prepared to contribute as much as 50% of the development cost of a particular project with the hope that it will recoup its investment by a levy on sales. (In this respect, NRDC's activities are unique. No other organization in the UK is known to undertake the support of a particular project within a firm in conditions which allow it to recoup its investment only by a levy on sales resulting from the successful outcome of that project. Grossfield³⁸ has discussed some of the merits of this and alternative systems of project finance.) The advantages of this scheme to the company are two-fold; first, projects can be undertaken on a risk-sharing basis in a situation in which, for one reason or another, the company does not feel it can underwrite the whole cost of development; second, it provides a method whereby a company can undertake development projects over and above those which it could finance from retained earnings or normal borrowing, possibly allowing the firm to broaden its product range more quickly. From the point of view of NRDC the investment is hopefully less risky because the development is carried out within the user company, and possibly more

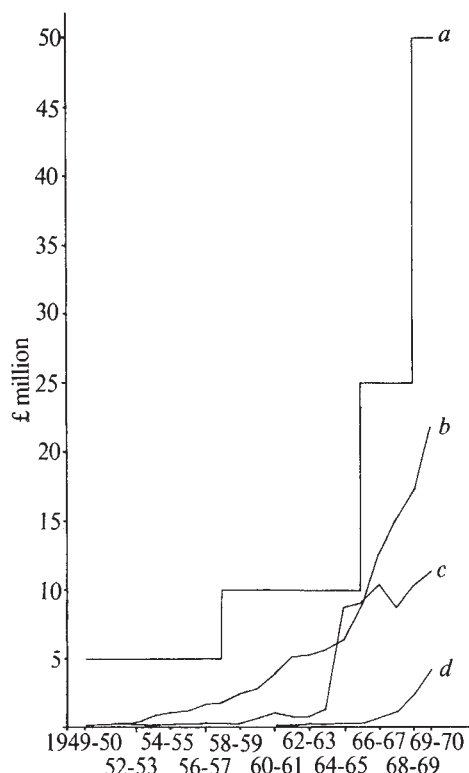


Fig. 3 Finances of NRDC (from annual reports). *a*, Government loan ceiling; *b*, cumulative government loan; *c*, additional forward commitments that year; *d*, total income. The cumulative loan is the difference between total incomes and outgoings. Total income includes sale of patent rights, revenues from exploitation of inventions and levies from joint venture projects.

profitable than some of the corporation's other activities, such as investment in start-up situations.

In the latter case, NRDC takes equity in the associated or subsidiary company—examples include Revenue Systems Ltd (46% holding), which is developing automated credit cards, and Tracked Hovercraft Ltd (100% holding) (see ref. 39 for a complete list). Although NRDC invests in these situations at an earlier stage of development than traditional institutions would usually consider, it presumably adopts very similar investment appraisal, selection and monitoring criteria. Indeed in some cases NRDC has invested in projects jointly with non-government funded institutions; for example, Technical Development Capital Ltd also holds equity in Revenue Systems Ltd.

The development of the NRDC in the context of British scientific and industrial institutions since the end of the Second World War can be seen in terms of a growing awareness of the complexities of technological innovation. It now seems clear that the continual stream of technological development, which forms an important basis for economic growth, cannot be obtained through the simple expedient of nurturing scientific and technical ideas in the hope that their commercial relevance will be apparent to the industrial sector. The temptation is very great to judge an idea or sophisticated gadget on its own merits, without adequate attention to its usefulness and its ultimate commercial viability. With the benefit of hindsight it is now evident that scientific and technical ideas must be seen as one element in the matrix of innovation—more consideration and effort in terms of both money and manpower must be expended in the production and marketing of ideas and hardware.

An apparent paradox, experienced by the NRDC over the last twenty years, thus emerges. On the one hand, there is no doubt that many eventually successful products are dependent on the use of sophisticated technologies and that these

should therefore be nurtured; on the other hand, the relationship between technology and the form of organization seeking to exploit it is so intimate that it could draw the government into almost every phase of its operations. In the present political climate, at least, this is regarded as undesirable. The simple fact seems to be that, considerations of national interest apart, it is difficult to see why projects which are judged to be commercially viable should need to be financed from public funds. The difficulty is to ensure that the community does not lose the potential benefits which might arise through innovations resulting from NRDC-type activities which produce a consumer surplus without any organization apparently obtaining any greater or smaller profits³⁸. Certainly the government's stated policy of disengagement from industry—witnessed by, for example, the disbandment of the Industrial Reorganization Corporation—is dependent (if industrial development is to continue) on private sources of capital acquiring the same kinds of expertise and taking the same kinds of calculated techno-economic risks that are now being taken by NRDC.

G. E. H. acknowledges a Science Research Council advanced course studentship in the Department of Liberal Studies in Science; D. S. W. holds a Midland Bank Finance Corporation research fellowship at the Manchester Business School Research and Development Research Unit.

¹ Select Committee on Science and Technology, *Carbon Fibres Report*, HC 157 (HMSO, 1969).

² House of Commons written answers, *Hansard* (February 17, 1971).

³ *Financial Times*, 6 (April 1, 1971).

⁴ *The Reorganisation of Central Government*, Cmnd. 4506 (HMSO, 1970).

⁵ *Industrial Research and Development in Government Laboratories* (HMSO, 1970).

⁶ Haigh, G. E., thesis, Univ. Manchester (1970).

⁷ *Problems of Scientific and Industrial Research*, 6 (Nuffield College, 1944).

⁸ Vig, N. J., *Science and Technology in British Politics* (Pergamon, Oxford, 1968).

⁹ *Swan Committee Report on the Patents and Designs Acts*, Cmnd. 7206 (1947) and Cmnd. 6789 (1946).

¹⁰ Hobhouse, L. T., *Science and Administration in Modern Government*, Memorial Trust Lectures, No. 14 (London, 1944).

¹¹ Larke, Sir W., *Industry and Research* (Federation Brit. Industries Conf., 1946).

¹² Attlee, C., *Hansard* (April 19, 1944).

¹³ Wilson, H., *Hansard* (June 11, 1944).

¹⁴ *Development of Inventions Act* (1948).

¹⁵ *Treasury Circular*, T.C. No. 5/50 (1950).

¹⁶ *NRDC Report and Statement of Accounts 1949/1950* (HMSO, 1951).

¹⁷ *NRDC Annual Report, 1953/4*, 2 (HMSO, 1955).

¹⁸ *Development of Inventions Act* (1954).

¹⁹ *Development of Inventions Act* (1958).

²⁰ Grossfield, K., *Econ. J.*, 72, 12 (1962).

²¹ Duckworth, J., *Economist*, 5 (January 4, 1964).

²² *Estimates Committee, Third Report*, 52 (1964/5).

²³ *NRDC Annual Report 1964/65* (HMSO, 1966).

²⁴ *Development of Inventions Act* (1965).

²⁵ *National Plan*, Cmnd. 2764, 49 (1964/5).

²⁶ *NRDC Annual Report 1964/65*, 6 (HMSO, 1967).

²⁷ Edwards, R. S., and Townsend, H., *Business Enterprise: Its Growth and Organisation*, 364 (Macmillan, 1965).

²⁸ Caplan, B., *New Scientist*, 326 (May 6, 1971).

²⁹ *Economist*, 85 (May 1, 1971).

³⁰ *Times Business News* (March 16, 1971) and reply by Dr B. Bard, NRDC managing director (March 22, 1971) and associated correspondence.

³¹ *NRDC Annual Report 1969/70* (HMSO, 1971).

³² Gibbons, M., and Watkins, D. S., *J. R. and D. Management*, 1, 11 (1970).

³³ Marshall, W., *The Role of Harwell in Industrial Research and Innovation*, Conf. industrial innovation through contract research, University of Newcastle upon Tyne, April 1970.

³⁴ *New Technology*, No. 33 (October 1969).

³⁵ *Selectivity and Concentration in Support of Research*, SRC pamphlet, 1-70 (Science Research Council, London, 1970).

³⁶ *Science Research Council Annual Report 1969/70* (HMSO, 1970).

³⁷ *NRDC Annual Report 1966/67*, 6 (HMSO, 1968).

³⁸ Grossfield, K., *National Provincial Bank Review*, 77, 6 (1967).

³⁹ *NRDC Annual Report 1969/70*, 79, 80 (HMSO, 1971).

Lithium in Psychiatry

I. B. PEARSON

University Department of Psychiatry, Sheffield S10 3TL

F. A. JENNER

MRC Unit for Metabolic Studies in Psychiatry, University Department of Psychiatry, Sheffield S10 3TL

Lithium salts have been reported to have valuable therapeutic effects in psychiatric disorders. But although some impressive results have been obtained, there is still much to be learnt about the effects and metabolism of lithium.

LITHIUM salts have been used medicinally in various ways for more than a century, and their history has been one of mistaken enthusiasm. Garrod recommended them for the treatment of kidney stones, gout and other rheumatic conditions in 1859¹, but without appreciable success. Subsequently lithium bromide was given as an anticonvulsant in the treatment of epilepsy, but it was no more effective than other bromides. At the end of the nineteenth century lithium salts were first tried in the treatment of mental illness. Lange² considered that lithium was helpful in mental depression, but fifty years were to elapse before further and more extensive psychiatric uses developed. More recently lithium salts have been offered as a substitute for sodium chloride in patients requiring a restricted sodium intake, but there were fatalities, and it is now recognized that cardiac and renal decompensation are both indications that the use of lithium should be avoided. Psychiatric interest was revived after work reported by Cade in 1949³ when, following an accidental observation of a sedative effect on guinea-pigs, lithium was found to be helpful in controlling mania. The modern psychotropic use of lithium dates from that time, but dissemination has been slow and probably reflects a natural caution after the earlier fatalities, combined with the introduction of many new and effective psychoactive compounds.

During the past two decades lithium has been used increasingly in the treatment of manic-depressive illnesses in which the mood of the patient is elevated in mania and lowered in depressions. Results so far suggest that lithium salts have considerable potential in the treatment of manic depressive illnesses, although it is far from clear how they exert their effects.

Very occasionally the patient's mood changes in a regular clock-like manner, but it is more usual to find only occasional brief episodes of mania interspersed in a series of depressive episodes. The remarkably regular patients, though very rare, offer unusual opportunities to prove that lithium salts have a psychopharmacological effect. This has been done, but the relevance of such findings to the more usual clinical studies requires a more complicated statistical approach, taking proper account of the variable natural history of the condition.

It is difficult to classify these illnesses since unipolar affective disorders are much commoner than the bipolar type, and patients who have recurrent episodes of depression for several years may then have a manic episode. Depressions also merge into anxiety and other psychiatric states. The natural history and heterogeneity of the clinical group studied present all sorts of obvious difficulties to the investigator, and it is these

types of problem which have influenced much of the debate about lithium in psychiatry. Schou, who produced a useful guide to the literature in 1968⁴, has been the most active and assiduous student in this field.

The effectiveness of lithium in the treatment of mania is now well recognized, and has been confirmed by controlled studies. But this treatment requires daily doses of the order of 1.5–2 g of lithium carbonate, when therapeutic and toxic levels closely approximate. In recent years the prophylactic use of lithium has been advocated, using rather smaller doses in the range 0.75 to 1 g daily of lithium carbonate, when toxic effects are reduced. The efficacy of lithium salts in the prophylaxis of manic depressive illness has been the subject of some debate. It has been claimed that when effective, lithium salts diminish the change in mood and in addition reduce the frequency of relapse in affective illness. Angst *et al.*⁵ have demonstrated a natural tendency in manic depressive illness for the frequency of episodes to increase, but the pattern of relapse in affective illness is variable, although it does tend to show a progression of increasing frequency which is greater in bipolar illness than in recurrent depressive illness.

Blackwell and Shepherd⁶ properly challenged some of the earlier favourable reports, pointing out that with such patients seen at a time of frequently recurring illness, a reduced rate of relapse might be accounted for solely by chance, and certainly this could be so with patients having frequent episodes, even if there is an overall tendency for the cycles to shorten. They suggested that the prophylactic value of lithium could only be determined by a comparative trial. Subsequently several clinical studies have been reported, including double blind trials, and most of them support the original conclusion that prophylactic lithium is of value. In general it seems that the frequency of relapse is appreciably reduced and that the natural trend of increasing frequency is reversed.

Lithium belongs to the group of alkali metals which includes sodium and potassium and it shares several properties with the other members of this group, but Birch has pointed out that in certain respects it resembles magnesium and calcium to which it bears a diagonal relationship in the periodic table⁷. It is absorbed promptly and virtually completely from the gastro-intestinal tract, and this is independent of whether lithium is given as carbonate, citrate or acetate. Lithium is not bound to plasma proteins, but is distributed freely in the tissues, and equilibration occurs, although this is somewhat slower in bone and brain. Distribution in the tissue differs sharply from that of sodium and potassium since lithium is more evenly divided between intracellular and extracellular compartments. Concentrations in the serum reflect those in tissue and can be used satisfactorily to monitor treatment. Lithium salts are largely excreted by the kidneys, and only small amounts are lost in faeces and sweat. Renal lithium excretion is proportional to the plasma concentration over a wide range; renal clearance is of the order of 15–30 ml./min, but decreases with age, and values of 10–15 ml./min are not uncommon in elderly people. Lithium excretion decreases when sodium intake is restricted.

The principal disadvantage of lithium therapy lies in the narrow safety margin between therapeutic and toxic doses. Therapeutic plasma concentrations are usually considered to

be between 0.8 and 1.6 mequiv./l.; at these concentrations only minor side effects occur. The commonest of these effects are gastro-intestinal disturbances, muscular weakness, tremor, drowsiness and a dazed feeling. When plasma concentrations are higher, serious toxic effects are liable to ensue, and poisoning results in coma, hyperreflexia, muscle tremor, attacks of hyperextension of the limbs and convulsions; fatalities have occurred. Haemodialysis is the most effective treatment if available but where this is not possible patients should be treated by forced diuresis. Long term treatment may give rise to small goitres and hypothyroidism but these usually respond to modest doses of thyroxine. Teratogenic effects have now been reported in two out of forty patients who received lithium during pregnancy⁸. Clearly lithium should be used with care, and concentrations in the blood should be monitored regularly.

Mode of Action

The mode of action of lithium in affective illness remains obscure, and most theories have related to interference in electrolyte metabolism or to effects on the metabolism of brain amines. More recently evidence has been adduced to suggest a specific effect of lithium on the limbic system of the brain, an area known to be associated with emotion⁹. These uncertainties about the action of lithium reflect the unsatisfactory state of understanding of the biological disturbance associated with manic-depressive illness.

When the fundamental importance of sodium and potassium for neuronal activity is considered together with the similarity of their ions to those of lithium, the suggestion that lithium interferes with the metabolism of these ions seems to be reasonable. Evidence is accumulating that disturbance of electrolyte and water balance accompanies manic-depressive illness although it is not clear whether this is causal or consequential. It has been shown that the administration of lithium leads to changes in the body water spaces, and this observation is supported by the natriuresis following the intake of lithium, which is more striking in normal people than in manic-depressive patients. More lithium is retained by patients than by normal people, and the retention is greater in mania and in patients who respond to lithium therapy. In addition a proportion of patients taking lithium develop persisting polyuria and thirst. This may be explained by the fact that lithium ions specifically and reversibly inhibit the action of the antidiuretic hormone on the kidney. Conceivably the consequences of this inhibition are relevant to the therapeutic effects.

Further work on this particular action has demonstrated that lithium probably blocks the action of the cyclic AMP released by vasopressin¹⁰. This raises the possibility that inhibition of the effect of vasopressin is just one example of an action on the effects of all hormones releasing cyclic AMP in target cells. In addition to its action on cyclic AMP, lithium also inhibits adenyl cyclase necessary for the production of cyclic AMP from ATP, but in the kidney this only occurs with high doses¹¹.

Perhaps a more exciting observation is an increase of α -ketoglutaric acid (shown by Bond *et al.*) in the urine of patients receiving lithium. This observation, although unequivocally established, still requires explanation. Does lithium, for example, inhibit enzymes in the tricarboxylic acid cycle and so cause a build-up of α -ketoglutaric acid? Is it a response to alkalosis and does it occur in brain? This, like many other questions, is being actively explored. It could also be relevant to Delgado and DeFeudis's observation⁹ that lithium leads to an increased level of brain glutamate.

Inhibition of several enzyme systems could be the result of effects of lithium on tissue magnesium and calcium which have now been observed. As these changes may also occur in brain, possible hypotheses of the consequences are legion.

The work of Smith, Balagura and Lubran¹² demonstrates an apparently direct action of lithium on the lateral nuclei of

the hypothalamus. There is stimulates drinking behaviour and presumably thirst. Application of lithium ions directly to the hippocampus and amygdala of monkeys⁹ evoked rather specific EEG effects which could be associated with the reduction of aggression reported in man, rodents and fish¹³⁻¹⁵. These are among the few reported direct effects of lithium on nervous tissue, and it is not surprising that neural function can be altered in this way, but the significance of these observations in relation to the therapeutic actions of lithium is not entirely clear.

Lithium does, however, have very clear effects on the electroencephalogram in man. In particular, it increases the amplitude of the alpha rhythm and causes slow waves to appear. After quite usual doses of lithium carbonate have been discontinued, the effects on the electroencephalogram persist for up to 6 weeks.

Lithium, like so many other agents which have therapeutic uses, is like a heavy spanner in a delicate piece of machinery. Like electroconvulsive therapy, it changes so many things that clues to as what is relevant are difficult to assess. Among other effects which require further study, one must include inhibition of carbohydrate transport¹⁶⁻¹⁸ across various membranes including the inhibition of the accumulation of myoinositol by the lens¹⁹ and kidney²⁰. The latter substance may well have a special role in the central nervous system.

The most popular current theories suggest that brain monoamine metabolism is altered in manic-depressive illness, but again, as with electrolytes, it is uncertain whether this is cause or effect; moreover, it is not clear which of the amines is related to changes in mood. Lithium has effects on brain monoamine metabolism, but these are confined to noradrenaline and the function of noradrenergic neurones. Noradrenaline metabolism is shifted from O-methylation to intraneuronal deamination with an increase in noradrenaline destruction; noradrenaline uptake by synaptosomes is increased and the release of synaptic neurotransmitters may be inhibited. Unfortunately these findings do not easily fit into models developed to account for the actions of psychotropic drugs, since such drugs change mood in one direction only, whereas lithium restricts mood swing in both directions. One school of thought, however, considers mania as a more profound form of depression²¹.

The pharmacological actions of lithium salts are curiously complex, and knowledge about them is far from complete. Indeed, there is ample room for further research designed to increase our understanding of the effects of lithium, which may in turn shed more light on the biological mechanisms possibly involved in manic-depressive illnesses.

¹ Garrod, A. B., *Gout and Rheumatic Gout* (Walton and Maberly, London, 1859), cited by Ottosson, J. O., *Acta Psychiat. Scand.*, Suppl. 207 (1969).

² Lange, C., *Bidrag til urinsyriediates ens klinik. Hospitalstidende*, 5, 1 (1897), cited by Ban, T., *Psychopharmacology* (Williams and Wilkins, 1969).

³ Cade, J. F. J., *Med. J. Austral.*, 36, 349 (1949).

⁴ Schou, M., *J. Psychiat. Res.*, 6, 67 (1968).

⁵ Angst, J., Weis, P., Grof, P., Baastrup, P. C., and Schou, M., *Brit. J. Psychiat.*, 116, 604 (1970).

⁶ Blackwell, B., and Shepherd, M., *Lancet*, i, 968 (1968).

⁷ Birch, N. J., *Brit. J. Psychiat.*, 116, 461 (1970).

⁸ Schou, M., and Amdisen, A., *Lancet*, i, 1391 (1970).

⁹ Delgado, J. M. R., and DeFeudis, F. V., *Exp. Neurol.*, 25, 255 (1969).

¹⁰ Harris, C. A., and Jenner, F. A., *J. Pharmacol.* (in the press, 1971).

¹¹ Dousa, T., and Hechter, O., *Life Sci.*, 9, 1, 765 (1970).

¹² Smith, D. F., Balagura, S., and Lubran, M., *Physiol. Behav.*, 6, 209 (1971).

¹³ Sheard, M. H., *Nature*, 230, 113 (1971).

¹⁴ Sheard, M. H., *Nature*, 228, 284 (1970).

¹⁵ Weischer, M. Z., *Psychopharmacologia*, 15, 245 (1969).

¹⁶ Bhattacharya, G., *Biochim. Biophys. Acta*, 93, 644 (1964).

¹⁷ Bihler, I., and Adamic, S., *Biochim. Biophys. Acta*, 135, 466 (1967).

¹⁸ Bosackova, J., and Crane, B. K., *Biochim. Biophys. Acta*, 102, 423 (1965).

¹⁹ Varma, S. D., Chakrapani, B., and Reddy, V. N., *Invest. Ophthalm.*, 9, 794 (1970).

²⁰ Margolis, R. U., and Heller, A., *Biochim. Biophys. Acta*, 98, 438 (1965).

²¹ Coppen, A., and Shaw, D. M., *Lancet*, ii, 805 (1967).

Perspectives in Organometallic Chemistry

F. G. A. STONE

School of Chemistry, University of Bristol

Professor Stone describes the state of the art of organometallic chemistry and suggests that it will continue to be a growth point in the chemical sciences.

ORGANOMETALLIC compounds are those substances containing organic groups attached to metal atoms by carbon-metal bonds. The metal may be from the main groups of the periodic table (for example, magnesium or lead), or it may be a transition element such as titanium or iron. The organic groups are of many different types and include both the familiar radicals of organic chemistry such as CH_3 or C_6H_5 which bond both to main group metals and to transition metals, and also stable molecules such as CO , C_2H_4 or C_6H_6 which can coordinate to transition metals. One of the many interesting facets of this field has been the discovery that transition metals can form stable bonds with entities such as cyclobutadiene or trimethylenemethane which are incapable of an independent existence. Countless organometallic compounds are known, and many have played an important role in the history, theory, technology and laboratory practice of chemistry. For example, the discovery^{1,2} of ferrocene *bis*(π -cyclopentadienyl)iron, ($\pi\text{-C}_5\text{H}_5$)₂Fe (Fig. 1), brought about a renaissance in the study of organo-derivatives of the transition metals. The elucidation³ of the polymeric structure of $[(\text{CH}_3)_2\text{Be}]_n$ did much to stimulate work on electron deficient compounds. In these the number

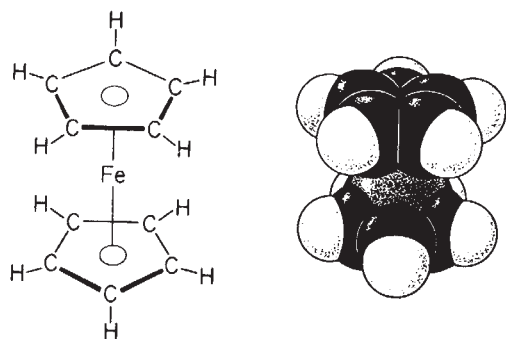


Fig. 1 The structure of ferrocene.

of bonding orbitals exceeds the number of available electron pairs, so that some bonding orbitals embrace more than two atoms—that is, they are multicentred. The Ziegler-Natta catalysts⁴ have had a profound effect on the technology of macromolecules, and organoboron compounds are now widely used in organic syntheses⁵.

In the chemical literature, references to organometallics first appeared in the early nineteenth century. In 1827 the Danish chemist Zeise^{6,7} found that boiling platinum chloride with ethanol and adding potassium chloride produced a substance of composition $\text{KCl}\cdot\text{PtCl}_2\cdot\text{C}_2\text{H}_4\cdot\text{H}_2\text{O}$. More than

100 years were to pass before it was realized that Zeise's salt should be formulated as a coordination compound of platinum, that is $\text{K}[\text{C}_2\text{H}_4\text{PtCl}_3]\cdot\text{H}_2\text{O}$, with carbon-metal bonding. Early historical landmarks were Bunsen's synthesis⁸ of cacodyl $(\text{CH}_3)_2\text{AsAs}(\text{CH}_3)_2$ in 1842, Frankland's synthesis⁹ of alkyl-zinc compounds in 1849, Mond's synthesis¹⁰ of nickel carbonyl $\text{Ni}(\text{CO})_4$ in 1890, and Grignard's discovery¹¹ of organomagnesium compounds (for example, $\text{C}_2\text{H}_5\text{MgBr}$) in 1900.

No account of recent developments in organometallic chemistry would be complete without a brief summary of current views on such matters as stability, bonding and structure. Indeed, it is in these areas that some of the most significant recent advances have been made. Studies in this field, as in organic chemistry, have been greatly aided by the application to structural problems of such techniques as nuclear magnetic resonance spectroscopy and single crystal X-ray crystallography. The discovery of many novel compounds with unusual bonding of organic groups to metals has done much to stimulate preparative work in this field. The application of valence theory, particularly consideration of molecular rather than atomic orbitals, has led to a better understanding of the reactivity of compounds with important consequences for further chemical syntheses.

Stability, Bonding and Structure

All organometallic compounds are thermodynamically unstable to oxidation, the driving force for which is the large favourable free energy change in the conversion into metal oxide, carbon dioxide and water. In this respect organometallic compounds are no different from purely organic compounds except that an additional product (metal oxide) is involved. As in organic chemistry, however, kinetic factors are often decisive in inhibiting oxidation in ambient conditions. Instability to air can often be associated with the presence of empty low lying metal orbitals which can interact with molecular oxygen thereby providing a pathway to decomposition involving little activation energy. Similar considerations apply to hydrolytic instability. Hydrolysis often proceeds by initial bonding of a water molecule, a process facilitated by an empty metal orbital which can accept an electron pair from the substrate. Thus the simpler organo-derivatives of lithium, beryllium or aluminium are readily, sometimes even explosively, decomposed by water or oxygen. The high reactivity can be traced to the ability of these metals first to coordinate a reactant molecule; this is followed by interaction of the bonded substrate with a polar carbon-metal bond. Indeed, whether or not decomposition follows attachment of a substrate molecule depends on the nature of the carbon-metal bond as determined by electronic and steric factors. With electropositive metals such as aluminium the bond may be

$\delta+ \quad \delta-$

sufficiently polar in the sense $\text{M}-\text{R}$ that the organic group becomes susceptible to electrophilic attack (for example, from a proton of coordinated water to release RH). Most organometallic compounds are, however, highly covalent in nature because the electronegativity differences between the organic

groups and the metal atoms are small. Indeed, the least electropositive metals, such as lead or mercury, form organo-derivatives (for example $(C_2H_5)_4Pb$ or $(CH_3)_2Hg$) which provide excellent examples of covalent compounds with classical two electron, two centre σ bonds. In accord with this they are volatile, hydrocarbon soluble and immiscible with water. By contrast with the behaviour of the light metals mentioned above, chromium forms a cationic benzyl complex $[C_6H_5CH_2Cr(H_2O)_5]^{2+}$ sufficiently stable to have a half-life of about 1.5 day in solution¹². Even though water molecules are present in the coordination sphere of the metal in the cation, the C–Cr σ bond is insufficiently polar to release the benzyl group as toluene. Addition of acid does, however, decompose the complex.

Carbon–mercury bonds form readily from mercury salts in a variety of reactions. These bonds once formed are relatively stable in ambient conditions because the R–Hg group has little affinity for oxygen or water. Organo-mercurials are very poisonous, and the chemical robustness of CH_3Hg and related groups can have serious consequences if they become accumulated in natural food chains through careless discharge of industrial waste. One process for converting acetylene into acetaldehyde depends on a mercury catalyst and effluent from a factory using this process was responsible for several deaths from the so-called Minamata Bay disease. Shellfish removed from the sea for human consumption were subsequently found to contain the compound CH_3HgSMe (ref. 13). The death of birds in Sweden was traced to the use of phenylmercury compounds in the pulp and paper industry; degradation produced elemental mercury which was converted to methylmercury by bacterial action—after ingestion into fish the mercury became concentrated in sea birds. Organomercury compounds have been used in fungicides used in the treatment of wheat and in this manner mercury has been transmitted to humans by way of hogs in New Mexico¹⁴.

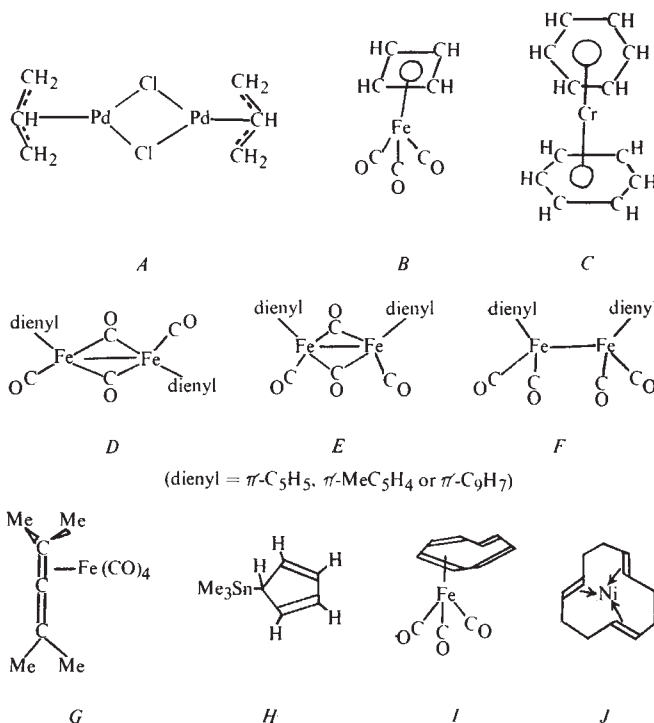
The thermal stability of organometallic compounds varies considerably. Some such as the tetraalkyl derivatives of tin or ferrocene are very stable. The last of these survives heating to over 400° C in the absence of air. The robustness of a particular organometallic can be related to the energy required to bring about loss of the organic group as a molecule or a radical and this in turn depends on the activation energy needed to promote a bonding electron from the highest filled molecular orbital of the compound into an anti-bonding orbital. In this way a molecule C_nH_n could dissociate from $\pi-C_nH_nM$, and a radical R, which could irreversibly dimerise to R_2 , might form from $\sigma-RM$ (where M is a metal atom with attendant ligands). In the last case an alternative mode of decomposition involves release of olefin through the reaction $\sigma-CH_3CH_2M \rightarrow C_2H_4 + HM$. The reverse of this reaction is important in the synthesis of organometallic compounds.

Evidently the energy required for decomposition is very small for a molecule such as $(CH_3)_4Ti$ which decomposes above –78° C, whereas it is high for a molecule such as ferrocene or $(Ph_3P)_2Pt(CH_3)_2$. Phosphines are especially effective ligands for stabilizing carbon–metal σ bonds and it has been suggested that they modify the relative energies of the orbitals so that the energy difference between the highest occupied and lowest unoccupied orbital is increased^{15,16}. The stability of ferrocene may be correlated with the complete electron occupation of all bonding orbitals (the iron atom acquires a pseudo-krypton electron configuration according to the “effective atomic number rule”) coupled with the relatively high energy of the anti-bonding orbitals, the transfer of electrons to which would destabilize the compound.

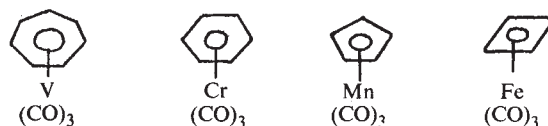
π -Complexes

Ferrocene^{17,18} is but one of many so-called “ π -complexes”, most of which have been prepared in the past ten or fifteen years. π -Complexes are coordination compounds in which unsaturated organic systems are associated with metals, which

may or may not have other ligands present. Examples include Zeise's salt (mentioned earlier), allylpalladium chloride^{19–21}, cyclobutadieneiron tricarbonyl²² and bis(benzene)-chromium²³ (Fig. 2A, B and C). Generally the bonding of these



unsaturated groups to the metals is interpreted in terms of donation of π electrons from the hydrocarbon into vacant d orbitals of the metal, coupled with transfer of electrons from the metal to the ligand by way of overlap of filled orbitals of the metal with empty anti-bonding (π^*) orbitals of the hydrocarbon. The components of the bond thus involve opposing electron flows and as such tend to strengthen one another (a synergic effect). This concept stems from consideration of the nature of the bonding of the ethylene to platinum in the anion of Zeise's salt $[(\pi-C_2H_4)PtCl_3]^-$ (refs. 24, 25). The overall effect on the stereochemistry of the complexes is that all the carbon atoms of the unsaturated systems are equivalently bonded to the metal atoms, for example



It follows that if retrodonative bonding is important for the existence of the compounds, metals will generally only form π -complexes when they are in low oxidation states because only then will filled d orbitals be available on the metal atoms to partake in bonding with π^* orbitals of the hydrocarbon groups. In support of this concept, it has been found experimentally that the new organic chemistry of the transition elements is most extensive when the metal is in a relatively low oxidation or valence state. Moreover, the discovery of countless π complexes has brought about a convergence of organometallic and coordination chemistry. Thus nickel is formally zerovalent not only in the well recognizable coordination complexes $K_4[Ni(CN)_4]$ and $Ni(PF_3)_4$ but also in the π -complex $Ni(\pi-C_8H_{12})_2$ (C_8H_{12} is cycloocta-1,5-diene).

Structural Studies

Although infrared and nuclear magnetic resonance (NMR) spectroscopy are used extensively in the study of organo-

metallic compounds, the increasing complexity of the complexes discovered makes the X-ray crystallographic method the final arbiter of structures. This analytical technique has been greatly facilitated by computer processing of data, and about 150 new organometallic structures are now determined by this technique each year. Important though the X-ray study of single crystals is, however, it has become increasingly clear in the past decade that the structure of an organometallic in the solid state is not necessarily the same as that operating in solution. This is because many of the molecules are stereochemically non-rigid. The intramolecular rearrangements can take two forms; the first involves tautomerism wherein non-equivalent structures are detectable, often by infrared spectroscopy. Thus the cyclopentadienyliron carbonyl complex $[\text{Fe}(\text{CO})_2(\pi\text{-C}_5\text{H}_5)]_2$ has the centro-symmetric structure (Fig. 2D) in the crystal with two bridging and two terminal CO ligands²⁶. The infrared spectra of this and related complexes (dienyl = $\pi\text{-MeC}_5\text{H}_4$ or $\pi\text{-C}_9\text{H}_7(\text{indenyl})$) in solution are, however, solvent dependent, and vary in a manner that indicates an equilibrium between the forms indicated in Fig. 2D, E and F; the last form is present only in small amounts²⁷. A second phenomenon, even more widely observed, involves interconversions between equivalent structures which are therefore of equal free energy content. Such molecules are termed fluxional²⁸; atoms of a given element exchange sites within the molecule at a speed which can be detected by n.m.r. spectroscopy. This spectroscopic technique operates on a time scale 10^{-1} to 10^{-9} s, similar to that of the dynamic processes whereby molecules pass from one configuration to another involving a different permutation of the nuclei.

Several types of fluxional organometallic molecules are known. An interesting example in the acyclic olefin category is the tetramethylallene complex²⁹ (Fig. 2G). The instantaneous structure shown should give rise to a proton NMR spectrum with three sets of resonances (relative intensity 1 : 1 : 2), whereas a single sharp signal is observed at 25° C. It is reasonable to assume that the $\text{Fe}(\text{CO})_4$ group moves from end to end of the allene group at a speed greater than the time scale of the NMR experiment. Such intramolecular processes should slow down when the temperature is lowered and in accord with this at -60° C the spectrum of the structure shown in Fig. 2G appears as the expected three signals.

Many non-transition metal and transition metal compounds containing σ -bonded cyclopolyene groups show fluxional behaviour. For example, the chemical behaviour of the cyclopentadienyl compound $\text{Me}_3\text{Sn}(\sigma\text{-C}_5\text{H}_5)$ (Fig. 2H) suggests the 1,3-diene system shown, which would imply three different environments for the protons. The spectrum nevertheless shows only a single peak indicating a rapid movement of the carbon-metal bond among the five possible positions.

Among the most intensively studied fluxional organometallics are those involving coordination of a cyclic polyolefin to a metal carbonyl group, the cyclic olefin having more π -electrons than the metal needs to achieve the effective atomic number rule (that is, 4 for the $\text{Fe}(\text{CO})_3$ group and 6 for the $\text{Mo}(\text{CO})_3$ group). A classic example of this behaviour is the cyclooctatetraene complex (Fig. 2I). The structure shown has been established in the crystal state by X-ray methods³⁰. The diffraction of X-rays takes place on a time scale of 10^{-18} s and so this technique "sees" the instantaneous structure. At room temperature the proton NMR spectrum of $(\pi\text{-C}_8\text{H}_8)\text{Fe}(\text{CO})_3$ shows a single peaking indicating that all protons are equivalent which is not in accord with a rigid structure as shown in Fig. 2I. Apparently the locus of the metal attachment to the four carbon atoms of the ring shifts at such a speed that the protons appear to be equivalent. On lowering the temperature to -150° C the spectrum becomes more complex; for example, that of the ruthenium analogue $(\pi\text{-C}_8\text{H}_8)\text{Ru}(\text{CO})_3$ displays four bands as the intramolecular rearrangement slows down^{31,32}. The mechanism by which this occurs—for example, a 1,2-shift of the $\text{M}(\text{CO})_3$ group around the ring, is not known with certainty partly because

of the experimental difficulties of knowing whether the limiting spectrum corresponding to rigidity has been reached even at $\sim -150^\circ\text{C}$ (ref. 33).

Chemical Reactivity

The rapid expansion of organometallic chemistry in recent years has had many important consequences which have stimulated research. It has become clear that there are numerous ways in which organic groups can be combined with metals and because metals vary so much in their chemistry, quite different properties are found for organometallic compounds involving the same organic group but different metallic elements. The extraordinary development of the organic chemistry of the transition metals has followed in part from the recognition that the properties of organometal groups are influenced by the presence of other ligands in the coordination sphere of the metal. In other words, because of their electronic and steric effects, particular ligands can act as fine tuners in determining the reactivity of others.

In dealing with such wide variations of chemical behaviour in the context of developments in recent years it is convenient to separate the organo-derivatives of the main group metals from those of the transition metals. Such a separation is, however, somewhat arbitrary because many compounds are known containing both main and sub-group metals associated with organic moieties.

Main Group Metals

During the first half of this century it became widely recognized that organolithium and organomagnesium compounds were valuable in synthesis. In 1956 it was discovered that diborane (B_2H_6), generated *in situ* from sodium borohydride and a boron halide, added rapidly to olefins in the presence of ether (for example, diglyme $(\text{CH}_3\text{OCH}_2\text{CH}_2)_2\text{O}$) (refs. 5, 34, 35).



It has been found possible to cleave the C-B bonds thus formed in a variety of ways, and this reaction, termed hydroboration, has become the basis of many organic syntheses comparable in importance with the earlier discovered Grignard and lithium reagents. Thus treatment of a triorganoborane with alkaline hydrogen peroxide yields an alcohol $\text{RCH}_2\text{CH}_2\text{-OH}$, whereas protonation by acid gives RCH_2CH_3 , that is, an overall hydrogenation of a double bond. Oxidation of $(\text{RCH}_2\text{CH}_2)_3\text{B}$ with chromic acid gives ketones or acids, whereas treatment with bromine and sodium methoxide gives $\text{RCH}_2\text{CH}_2\text{Br}$ (an overall anti-Markownikov addition of HBr to $\text{RCH} : \text{CH}_2$). Many related organic syntheses depend on the hydroboration of acetylenes or dienes as the first step, and with olefins, acetylenes or dienes the substituents on the double or triple bonds can be complex organic groups so that the reaction has very wide scope throughout organic chemistry.

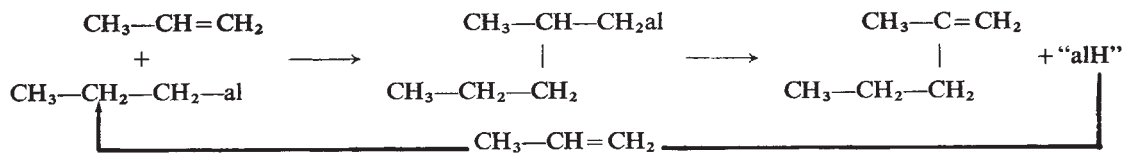
Hydroboration is formally related to the so-called "direct syntheses" of aluminium alkyls developed by Ziegler and his coworkers⁴:



Moreover, aluminium alkyls themselves react with olefins in a stepwise growth reaction:



As aluminium alkyls are readily oxidized to alcoholates $(\text{RO})_3\text{Al}$ which in turn can be hydrolysed, this process forms the basis for a conversion of ethylene into long chain primary alcohols. The importance of the aluminium alkyls does not, however, end with the synthesis of alcohols needed for the detergent industry. Propylene when heated with tripropylaluminium under pressure is converted into 2-methyl-1-pentene



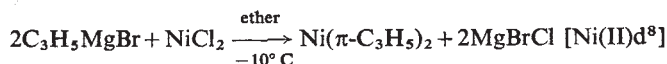
((C₃H₇)₂AlH = alH)

Rearrangement of 2-methyl-1-pentene into 2-methyl-2-pentene followed by elimination of methane by cracking affords the important monomer isoprene (synthetic rubber).

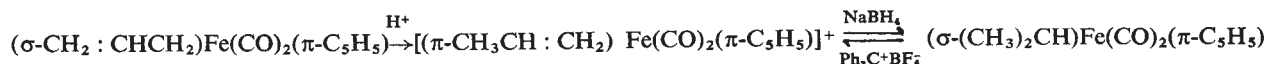
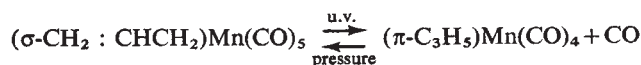
Transition Metals

Spurred by the recognition of the sandwich structure of ferrocene and the discovery within the following decade of such compounds as dibenzene chromium (Fig. 2c, ref. 23) and cyclododeca-1,5,9-trienenickel (Fig. 2J, refs. 36, 37), new organo-complexes of the transition metals were characterized very rapidly³⁸. This period of research activity was accompanied by a growing awareness of the many ramifications of this field. Among the more important of these may be mentioned the following.

(i) It is relatively easy to prepare metal complexes containing hydrocarbon groups if certain other ligands are also present, particularly carbon monoxide and phosphine groups. Moreover, it is also possible to prepare complexes containing only hydrocarbon ligands if either the metal is preconditioned by a reductive process in the presence of a hydrocarbon which then uses its π electrons to fill the metal's bonding orbitals, or a salt is treated with a suitable carbanion so that in the organometallic produced the metal remains in the same stable valence state. Such syntheses are illustrated by the preparation of the nickel complex Ni(π -C₈H₁₂)₂ by reducing nickel acetylacetonate with aluminium alkyls in the presence of cycloocta-1,5-diene (ref. 39), and the preparation of *bis*-(π -allyl)nickel by the reaction⁴⁰



(ii) The mode of bonding of an organic group to a metal can change from the σ to the π form or vice versa, for example



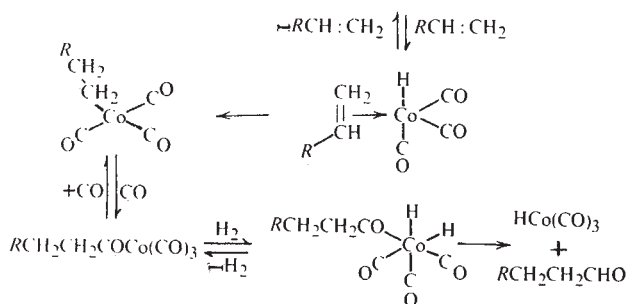
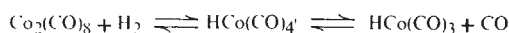
Such transformations are the key to certain catalytic reactions of technological importance to be described later. Moreover, these rearrangements fall into the category of reactions of coordinated ligands, an area of coordination chemistry which has been developed significantly in recent times⁴¹.

(iii) It has been amply demonstrated that reactions can be carried out on organic groups coordinated to transition metals, and indeed the metal can either donate or withdraw electron density from an organic moiety so that its substituent effect is profound. Metals are also multisite substituents with the sites disposed in accord with the metal's coordination characteristics. There has been a growing appreciation of the chemical consequences of the control of organic reactions by metals in the past decade, so that the mechanisms of a number of processes catalysed by transition metals are better understood; and some principles have been developed which have made the search for new catalysts less empirical.

Even before the discovery of ferrocene and related π -complexes, it was known that some organic syntheses were catalysed by transition metal complexes. Roelen⁴² studied the mechanism of the Fischer-Tropsch synthesis and discovered the oxo or hydroformylation reaction which generates aldehydes and alcohols from olefins, carbon monoxide, and hydrogen in the presence of cobalt catalysts. Reppe *et al.*⁴³

discovered that acetylene in the presence of nickel compounds can be cyclized to cyclooctatetraene and almost concurrently with the isolation of ferrocene, Ziegler *et al.*⁴⁴ found that the addition of transition metal halides to triethylaluminium produced a catalyst capable of polymerizing ethylene or propylene under mild conditions; this polymerization occurs in a sterically regular way⁴⁵. It has come to be recognized recently that all these processes have in common one of the most basic of all ligand reactions, namely the combination of two ligands within the coordination sphere of the metal in a so-called "insertion" step. This is well illustrated by the presently favoured mechanism for hydroformylation⁴⁶ shown in the scheme below. The catalyst is believed to be the hydrido-carbonyl HCo(CO)₃ which can bond an olefin molecule to form a π -complex because the cobalt atom is only four-coordinate ("coordinatively unsaturated"). Addition of the Co-H bond to the olefinic double bond affords an alkylcobalt tricarbonyl in an insertion step which involves rearrangement of a π into a σ -complex. The σ -complex is again coordinatively unsaturated, and reacts with CO to give an acylcobalt tricarbonyl in another insertion reaction. From mechanistic studies this is more properly regarded as a migration step in which an attacking CO ligand bonds to a vacant site on the cobalt atom thereby promoting transfer of the RCH₂CH₂ group onto one of the terminal CO ligands. The acylcobalt tricarbonyl complex involves Co^I(d⁸) and as such is able to cleave hydrogen molecules to form, by so-called oxidative addition, a cobalt (III) (d⁶) complex in which the components necessary to produce the aldehyde and regenerate the catalyst are brought together in close proximity in the metal's coordination sphere.

The generality of the insertion process is evident from the fact that it may be used to explain the function of the Ziegler-Natta catalysts. Stereospecific coordination of an olefin molecule to a vacant site on a titanium atom adjacent to a σ -bonded growing polymer chain can continue indefinitely for as long as the coordination step is followed by an insertion.



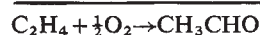
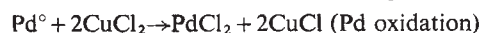
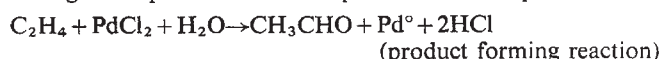
Catalysis

Studies on hydroformylation, hydrogenation and isomerization of olefins, and the oligomerization of dienes and acetylenes by transition metal complexes have, in the past, been predominantly empirical in nature in that one of a wide range of complexes tested has been found capable of promoting a certain type of reaction. As yet we are far from being able

to design catalysts for a given purpose because knowledge of the kinetic and thermodynamic factors which lead to formation of a complex and its subsequent breakdown in a desired way is too imprecise. Recent work has, however, amply demonstrated the importance of vacant coordination sites, σ - π transformations of organic groups, the widespread occurrence of insertion reactions—in particular those involving metal-hydrogen and metal-alkyl bonds—and the fact that there are a large group of syntheses which depend on the ability of transition metals to pass readily from one oxidation state to another. A good example of this ability is provided by the compound $(\text{Ph}_3\text{P})_3\text{RhCl}$, an effective hydrogenation catalyst which operates because rhodium(I) bonds olefins and can readily be "oxidized" by molecular hydrogen to a rhodium(III) hydrido-species which transfers hydrogen to an olefin molecule so that the catalyst is regenerated^{47,48}.

Many of the principles now associated with the reactions of organic groups bonded to transition metals are also applicable to biological processes where "metal-containing" enzymes catalyse isomerization and transmethylation reactions. As yet there is little evidence that metal-carbon bonds play any extensive role in biological chemistry though vitamin B_{12} forms C-Co bonds in its conversion to coenzymes (ref. 49 and references therein). In biological processes involving metals, the important ligand atoms are nitrogen and oxygen, but as both areas are part of the broader field of coordination chemistry as such, the study of one is likely to have some relevance to the other. And in the context of reactions of coordinated ligands, irrespective of whether metal-carbon, metal-nitrogen, or metal-oxygen bonds are involved, recent studies have shown that metal ions can assist either nucleophilic or electrophilic attack on a ligand depending whether the metal is in an electron-withdrawing or an electron-donating environment. These characteristics depend on the metal involved, its oxidation state, and also on the nature of all the ligands, and almost infinite variations in reactivity seem possible.

Olefins are not normally subject to nucleophilic attack. By contrast, coordination of, for example, ethylene to Pd^{+2} makes possible a reaction with water to yield acetaldehyde. This is the basis of the technologically important Wacker process^{50,51}. The overall reaction $(\text{C}_2\text{H}_4 + \frac{1}{2}\text{O}_2 \rightarrow \text{CH}_3\text{CHO})$ results from a combination of several steps. Thus in one variation of this basic reaction, ethylene and oxygen are passed through an aqueous solution of palladium and cupric salt.



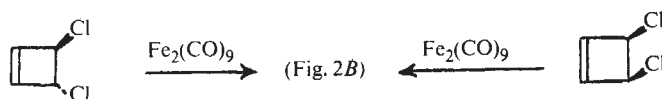
In the first reaction it is assumed that $[(\pi\text{-C}_2\text{H}_4)\text{PdCl}_3]^-$, closely related to the anion of Zeise's salt, is an intermediate. Ligand exchange of H_2O for Cl^- then gives $[(\pi\text{-C}_2\text{H}_4)\text{Pd}(\text{H}_2\text{O})\text{Cl}_2]$ which releases a proton (H_3O^+) and affords $[(\pi\text{-C}_2\text{H}_4)\text{PdCl}_2\text{-(OH)}]^-$. In the last of these species ethylene donates π -electrons to an electron accepting palladium (oxidation state +2) thereby promoting nucleophilic attack of OH^- (already within the metal's coordination sphere) on one of the carbon atoms to give a σ -bonded organo-palladium intermediate $[\sigma\text{-CH}_2\text{-OHCH}_2\text{PdCl}_2]^-$. The nominally vacant coordination site (it may be solvent occupied) on palladium would subsequently promote transfer of a β hydrogen atom, by way of transient Pd-H , to give an unstable carbonium ion $\text{CH}_3\text{C}^+(\text{H})(\text{OH})$ which affords acetaldehyde and a proton (hence HCl). Palladium metal is also formed and is reoxidized by cupric chloride. Addition of acetic acid as a reactant leads to the formation of vinyl acetate by attack of OAc^- on coordinated ethylene. Vinyl acetate is important as a monomer for lattices in paints, fibres and resins. Unfortunately there are important corrosion problems in its production by the liquid-phase palladium chloride process.

In other reactions π -complexes are susceptible to electrophilic rather than nucleophilic attack. In these cases the metal is in a low oxidation state so that electron density is available for transfer to the π^* orbitals of the ligand which thus becomes susceptible to Friedel-Crafts type substitutions, protonation or loss of hydride. The latter process, first reported in 1958 (ref. 52) has been used extensively in organometallic syntheses. For example, cycloheptatrienemolybdenum tricarbonyl reacts with trityl borofluoride $\text{Ph}_3\text{C}^+\text{BF}_4^-$ to give Ph_3CH and the cationic complex $[(\pi\text{-C}_7\text{H}_7)\text{Mo}(\text{CO})_3]^+$. Interestingly, in the cation the effect of the metal, now in a more positive oxidation state, is to make the C_7H_7 group susceptible to attack by nucleophiles (for example, R^-CN^- , OMe^- , Ph^- and so on) thereby producing cycloheptatriene derivatives $(\pi\text{-RC}_7\text{H}_7)\text{Mo}(\text{CO})_3$ (ref. 53).

Many olefin-metal complexes can be protonated³⁸ so that a hydrogen atom becomes attached to the hydrocarbon group. As well as rendering an olefin susceptible to protonation it is probable that the metal plays a rather direct role, through metal-hydrogen bond formation, in transferring the proton to the ring^{54,55}. Much research needs to be done to establish mechanistic details of metal-assisted electrophilic reactions in general, but it is clear that reactions of this kind have considerable potential in organic syntheses. Thus cyclooctatetraene does not undergo electrophilic reactions to give substituted derivatives. This is not true for cyclooctatetraene-iron tricarbonyl which undergoes both addition and substitution reactions with electrophiles (for example, POCl_3 in dimethylformamide, or CH_3COCl and AlCl_3) to give cyclooctatetraene derivatives coordinated to an $\text{Fe}(\text{CO})_3$ group⁵⁶. Treatment of the products with ceric salts liberates the substituted cyclooctatetraene. Pettit and his coworkers⁵⁷ first used this method for removing coordinated olefins from metals, and subsequently applied the technique in elegant studies on cyclobutadiene and its derivatives^{58,59}.

Cyclobutadiene Chemistry

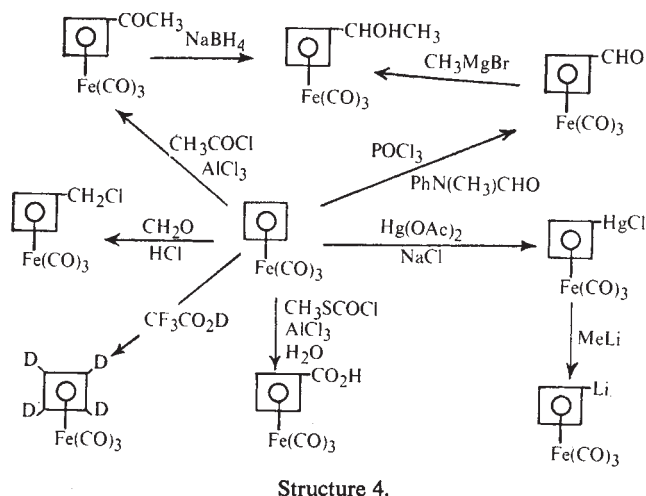
Mention was made earlier of the advances in organometallic chemistry which have led to the isolation of normally unstable organic moieties by coordination to a transition metal. The practical and theoretical problems associated with the cyclobutadiene molecule have concerned organic chemists for a hundred years. In perhaps the only example in organometallic chemistry where theory has been used to predict an experimental result, instead of accounting for it after it has been observed, Longuet-Higgins and Orgel⁶⁰ suggested that in spite of the instability of cyclobutadiene itself it would act as a good ligand. This suggestion was confirmed by the isolation of a stable tricarbonyliron complex of tetraphenylbutadiene by a serendipitous method⁶¹ (many of the best discoveries in the field have been made by chance), and by the characterization of a dimeric form (bridging chloride ligands) of tetramethylcyclobutadiene-nickel (ref. 62). The parent ligand was prepared by the synthesis^{58,59}



Cyclobutadieneiron tricarbonyl is an aromatic system in that it readily undergoes electrophilic substitution reactions. Moreover, the substituents introduced in this way undergo functional group chemistry without destabilization of the iron-cyclobutadiene bond (see structure 4).

The oxidative decomposition of cyclobutadieneiron tricarbonyl with Ce^{4+} has revealed several novel compounds through Diels-Alder type reactions, as indicated in Fig. 3.

The product from phenylacetylene is a molecule in which one ring has the Dewar benzene structure whereas the other has the Kekulé structure. Although this is somewhat of a laboratory curiosity, cyclobutadiene-iron tricarbonyl chemistry



does have considerable potential in organic syntheses. Thus in recent years there has been much interest in cubane chemistry, and this synthesis of a dicarboxylic acid derivative is relatively simple. The ring system has previously been accessible only by elaborate reaction sequences.

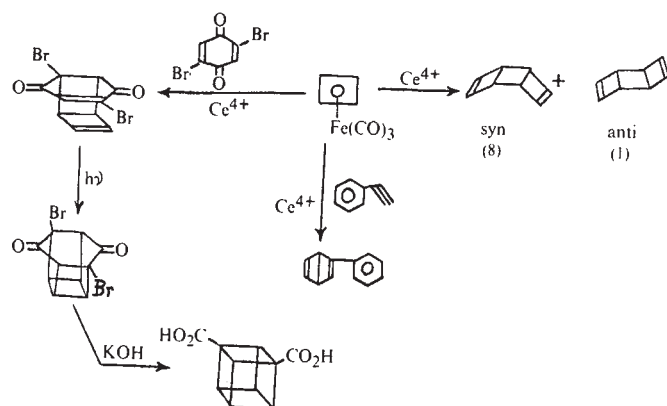


Fig. 3 Compounds revealed by the oxidative decomposition of cyclobutadieneiron tricarbonyl.

Predicting the Future

Although only a few organometallic compounds are widely used for specific purposes (for example, silicone polymers, tetraalkyl leads), their value in synthesis either as intermediates or as catalysts is great, and likely to increase in the future; and as organometallic chemistry impinges on both inorganic and organic chemistry research in this area helps to unify chemistry. But many problems remain to be solved. Previously insufficient attention has been given to a mechanistic approach in the study of organometallic reactions. Our knowledge of the bonding in organometallic compounds, particularly those involving transition elements, remains at best imprecise. Although some significant advances have been made in the design of homogeneous catalysts often little is known about the exact composition of the catalysts under the working conditions. Studies of a synthetic and structural nature of polynuclear metal complexes containing hydrogen and organic groups as ligands may eventually allow a better understanding of heterogeneous reactions, particularly the reactions of hydrocarbons on metal and metal oxide surfaces. It is difficult to predict the future of this field but it certainly has more momentum than many areas of chemistry.

- ⁴ Ziegler, K., *Adv. Organometal. Chem.*, **6**, 1 (1968).
- ⁵ Brown, H. C., *Hydroboration* (Benjamin, New York, 1962).
- ⁶ Zeise, W. C., *Pogg. Ann.*, **9**, 632 (1827).
- ⁷ Zeise, W. C., *Pogg. Ann.*, **21**, 497 (1831).
- ⁸ Bunsen, R., *Annalen*, **42**, 14 (1842).
- ⁹ Frankland, E., *Annalen*, **71**, 171, 213 (1849).
- ¹⁰ Mond, L., Langer, C., and Quincke, F., *J. Chem. Soc.*, 749 (1890).
- ¹¹ Grignard, V., *CR Acad. Sci.*, **130**, 1322 (1900).
- ¹² Anet, F. A. L., and Leblanc, E., *J. Amer. Chem. Soc.*, **79**, 2649 (1957).
- ¹³ Ue, J., and Kitamura, S., *Marine Pollution Bull.*, **2**, 56 (1971).
- ¹⁴ Curley, A., Sedlak, V. A., Girling, E. F., Hawk, R. E., Barthel, W., Pierce, P. E., and Likosky, W. H., *Science*, **172**, 65 (1971).
- ¹⁵ Chatt, J., *Proc. Chem. Soc.*, 318 (1962).
- ¹⁶ Chatt, J., *Record Chem. Prog.*, **21**, 147 (1960).
- ¹⁷ Wilkinson, G., Rosenblum, M., Whiting, M. C., and Woodward, R. B., *J. Amer. Chem. Soc.*, **74**, 2125 (1952).
- ¹⁸ Fischer, E. O., and Pfab, W., *Z. Naturforsch.*, **7b**, 377 (1952).
- ¹⁹ Moiseev, I. I., Federovskaya, E. A., and Syркин, Y. K., *Russ. J. Inorg. Chem.*, **4**, 1218 (1959).
- ²⁰ Smidt, J., and Hafner, W., *Angew. Chem.*, **71**, 284 (1959).
- ²¹ Hüttel, R., Kratzer, J., and Beckter, M., *Angew. Chem.*, **75**, 456 (1959).
- ²² Emerson, G. F., Watts, L., and Pettit, R., *J. Amer. Chem. Soc.*, **87**, 132 (1965).
- ²³ Fischer, E. O., and Hafner, W., *Z. Naturforsch.*, **10b**, 665 (1955).
- ²⁴ Chatt, J., and Duncanson, L. A., *J. Chem. Soc.*, 2939 (1953).
- ²⁵ Dewar, M. J. S., *Bull. Soc. Chim. France*, **18**, C79 (1951).
- ²⁶ Mills, O. S., *Acta Cryst.*, **11**, 620 (1958).
- ²⁷ McArdle, P. A., and Manning, A. R., *J. Chem. Soc.*, A, 1498 (1969).
- ²⁸ Cotton, F. A., *Accnts. Chem. Res.*, **1**, 257 (1968).
- ²⁹ Ben-Shoshan, R., and Pettit, R., *J. Amer. Chem. Soc.*, **89**, 2231 (1967).
- ³⁰ Dickens, B., and Lipscomb, W. N., *J. Chem. Phys.*, **37**, 2084 (1962).
- ³¹ Bruce, M. I., Cooke, M., Green, M., and Stone, F. G. A., *Chem. Commun.*, 523 (1967).
- ³² Bratton, W. K., Cotton, F. A., Davison, A., Musco, A., and Faller, J. W., *Proc. Nat. Acad. Sci.*, **58**, 1324 (1967).
- ³³ Cooke, M., Goodfellow, R. J., Green, M., Maher, J. P., and Yandle, J. R., *Chem. Commun.*, 565 (1970).
- ³⁴ Brown, H. C., and Subba Rao, B. C., *J. Amer. Chem. Soc.*, **78**, 5694 (1956).
- ³⁵ Brown, H. C., and Subba Rao, B. C., *J. Org. Chem.*, **22**, 1136 (1957).
- ³⁶ Wilke, G., *Angew. Chem.*, **72**, 581 (1960).
- ³⁷ Wilke, G., et al., *Angew. Chem. Internat. Ed.*, **2**, 105 (1963).
- ³⁸ Green, M. L. H., *Organometallic Compounds*, **2**, *The Transition Elements* (Methuen, 1968).
- ³⁹ Bogdanovic, B., Kroner, M., and Wilke, G., *Annalen*, **699**, 1 (1966).
- ⁴⁰ Wilke, G., and Bogdanovic, B., *Angew. Chem.*, **73**, 756 (1961).
- ⁴¹ Busch, D. H., *Science*, **171**, 241 (1971).
- ⁴² Roelen, O., *Angew. Chem.*, **60**, 62 (1948).
- ⁴³ Reppe, W., Schlichting, O., Klager, K., and Toepel, T., *Annalen*, **560**, 1 (1948).
- ⁴⁴ Ziegler, K., *Angew. Chem.*, **76**, 545 (1964).
- ⁴⁵ Natta, G., *Angew. Chem.*, **76**, 553 (1964).
- ⁴⁶ Heck, R. F., *Accnts. Chem. Res.*, **2**, 10 (1969).
- ⁴⁷ Montelatici, S., van der Ent, A., Osborn, J. A., and Wilkinson, G., *J. Chem. Soc.*, A, 1054 (1968).
- ⁴⁸ Osborn, J. A., Jardine, F. H., Young, J. F., and Wilkinson, G., *J. Chem. Soc.*, A, 1711 (1966).
- ⁴⁹ Parshall, G. W., and Mrowca, J. J., *Adv. Organometal. Chem.*, **7**, 203 (1968).
- ⁵⁰ Smidt, J., Hafner, W., Jira, R., Sieber, R., Sedlmeier, J., and Sabel, A., *Angew. Chem. Intern. Edn.*, **80** (1962).
- ⁵¹ Aguilo, A., *Adv. Organometal. Chem.*, **5**, 321 (1967).
- ⁵² Dauben, H. J., and Honnen, L. R., *J. Amer. Chem. Soc.*, **80**, 5570 (1958).
- ⁵³ Munro, J. D., and Pauson, P. L., *J. Chem. Soc.*, 3475, 3479, 3484 (1961).
- ⁵⁴ Winstein, S., Kaesz, H. D., Kreiter, C. G., and Friedrich, E. C., *J. Amer. Chem. Soc.*, **87**, 3267 (1965).
- ⁵⁵ Young, D. A. T., Holmes, J. R., and Kaesz, H. D., *J. Amer. Chem. Soc.*, **91**, 6968 (1969).
- ⁵⁶ Johnson, B. F. G., Lewis, J., and Randall, G. L. P., *J. Chem. Soc.*, A, 422 (1971).
- ⁵⁷ Pettit, R., and Emerson, G. F., *Adv. Organometal. Chem.*, **1**, 1 (1964).
- ⁵⁸ Pettit, R., *Pure Appl. Chem.*, **17**, 253 (1968).
- ⁵⁹ Ward, J. S., and Pettit, R., *J. Amer. Chem. Soc.*, **93**, 263 (1971).
- ⁶⁰ Longuet-Higgins, H. C., and Orgel, L. E., *J. Chem. Soc.*, 1969 (1956).
- ⁶¹ Hübel, W., and Braye, E. H., *J. Inorg. Nucl. Chem.*, **10**, 250 (1959).
- ⁶² Criegee, R., and Schröder, G., *Annalen*, **623**, 1 (1959).

¹ Miller, S. A., Tebbboth, J. A., and Tremaine, J. F., *J. Chem. Soc.*, 632 (1952).

² Kealy, T. J., and Pauson, P. L., *Nature*, **168**, 1039 (1951).

³ Rundle, R. E., *J. Phys. Chem.*, **61**, 45 (1957).

Lightning Observations by Satellite

J. G. SPARROW & E. P. NEY

School of Physics and Astronomy, University of Minnesota, Minneapolis, Minnesota 55455

The data from OSO-5 confirm the OSO-2 result that storm complexes at night are chiefly found over land. The North Atlantic Ocean seems to have more lightning storms associated with it than other regions of ocean whereas the principal desert regions display a marked scarcity.

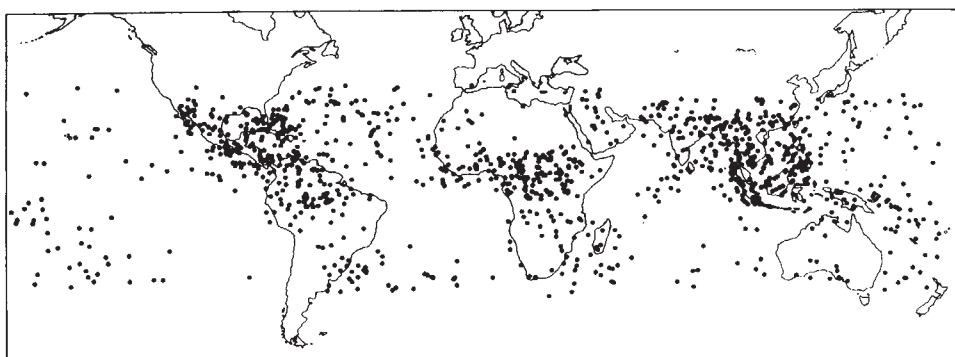
OBSERVATIONS of the positions of night-time lightning storms during the new Moon periods from February to October 1965 have already been reported¹ from the satellite OSO-2. A similar instrument was also flown on OSO-5, launched in January 1969, and this article reports the new data.

the light level is above a minimum value. This effectively limits the observational periods to times near new Moon.

Storm Complexes

The data were searched by the computer (CDC 6600) to separate abrupt increases that might be interpreted as lightning. Manual examination further refined the selection, taking into account the expected time constant of the signal decay, and the positions of lightning storm complexes were plotted. These were taken to be areas (several square degrees) containing one or more active lightning cells which gave rise to two or more lightning flashes visible at the satellite. This criterion (to reject a single flash seen by two telescopes) became necessary to remove some abrupt increases in the apparent light level that cannot be interpreted as lightning. The distribution of the lightning storm complexes (Fig. 1) is similar to that found previously, confirming the result from OSO-2 that the distribution of night-time storms is heavily biased towards land

Fig. 1 Distribution of night-time lightning storm complexes observed by photometers on board satellite OSO-5.



The Minnesota experiment⁴ on OSO-5 consisted of six photometers, four of which can be used to detect lightning strokes. This analysis is based on data from two of these, each having a 10° angular diameter field of view looking along the spin axis of the satellite in the direction opposite to that of the solar sail. Each photometer is sensitive to a broad spectral region, astronomical blue (approximately 3500 to 5000 Å) and red (approximately 6000 to 8000 Å) respectively. The photometers are sampled three and two times per 0.32 s when the satellite is in darkness. The time constants of the two telescopes are each approximately 0.1 s. The photometers are protected from excessive light levels by protective photo-diodes which disconnect the high voltage supply at times when

areas rather than similar areas of sea. As the satellite coverage is relatively uniform in bands of constant latitude, Fig. 1 may be interpreted directly as an indication of non-uniformity. About 1,000 storm complexes have been plotted in Fig. 1 from the data on some 7,000 lightning strokes. As the results from the new Moon period February to September 1969 (20 to 24 h local time) were similar to those from January to July 1970 (00 to 04 hLT), the data have been combined in one plot.

It is evident that these data are in agreement with Schonland's statement² that "thunderstorms are not very frequent over the oceans; exceptions are the areas off the south-east coasts of Brazil and South Africa, and the seas surrounding the islands of the East Indies and Madagascar". It is also apparent that

the North Atlantic Ocean has more lightning storms than similar areas of other oceans. There is a marked scarcity of lightning storms in the principal desert regions (Sahara and Kalahari Deserts, Great Australian Desert and the area in central South America) even compared with those over the North Atlantic Ocean.

The field of view of the photometers on the Earth ranges from approximately one square degree when the photometers view vertically to a maximum value of approximately 12 square degrees just before the field of view leaves the Earth. From the total time scan (~ 200 h) and the area-time scan (~ 400 degree² h) the mean area of the field of view is found to be approximately 2 square degrees. The number of lightning strokes in each storm complex varied from a minimum value of two to about thirty strokes seen in 2 min; most of the last group were observed simultaneously by both telescopes.

Spurious Events

On some occasions apparent "lightning strokes" were detected that could not be assigned as such because at the time the fields of view of the telescopes were well above the Earth. Some of these were detected by as many as three photometers simultaneously when the photometers were looking above the satellite. The decay time indicates that the signal probably originated forward of or in the photomultiplier preamplifier systems. Because the electronics associated with each photomultiplier are isolated from each other (although sharing the primary spacecraft power) it is unlikely that these apparent increases are electronic in nature. Furthermore, if the increases were initiated by feedback through the spacecraft batteries then all six photometers would probably show similar effects. This has occurred at other times when noise is present in the data but in these cases the characteristic time constant is not seen in each photometer signal. On the occasions under discussion, only those photometers viewing in the anti-sail direction and not those viewing in the opposite direction have been affected. The possibility of spurious reflexions from the front light baffles of each photometer (for example, from lightning, meteors and so on) can probably be eliminated because of the large attenuation in the scattered signal compared with the direct signal when the photometers view close to the Moon. The distribution of these signals over the Earth's surface is approximately random, suggesting that the source is not lightning. Single occurrences are seen about once every ten orbits. No acceptable mechanism has yet been found to explain these anomalous data spikes.

These increases, which seem to be due to short duration (< 0.1 s) "light" flashes, arise from processes other than lightning and must be eliminated from the data before any discussion of lightning distribution can be entered into. This has effectively been done by accepting as storms only those occasions when two or more strokes were observed. In this way some seventy occasions when one stroke only was seen simultaneously by the two telescopes—when their fields of view were on the Earth—have been eliminated.

No Change in Frequency

The earlier experiment on OSO-2 was conducted during solar minimum conditions (1965) whereas these later measurements were made at a more active solar period. If a substantial change in the worldwide frequency of night-time lightning storms occurred between these two periods it should be detectable from a comparison of the frequencies observed by the two satellites. That such a relation might exist between solar activity and increased storminess has been suggested by Ney³. Taking into account the increased sensitivity in the later experiment it does not seem that any significant change was detected (the accuracy of the comparison is not better than perhaps a factor of two). A search for solar activity effects can also be made by looking for a correlation between lightning

storm occurrence and K_p or another magnetic index within the data from one of these experiments. No significant correlation was found for lag/lead times of as much as 24 h between the time of storm occurrence and the three hourly value of K_p in the data of this experiment or in the less statistical data of OSO-2. These findings are not unexpected, for Markson⁴ has shown, from data supplied by Lethbridge, that there is no apparent correlation between annual thunderstorm activity in the US and the solar cycle. Brooks⁵ and Likhter *et al.* (quoted by Markson⁴) have also shown that there is low correlation between these parameters for low latitude stations.

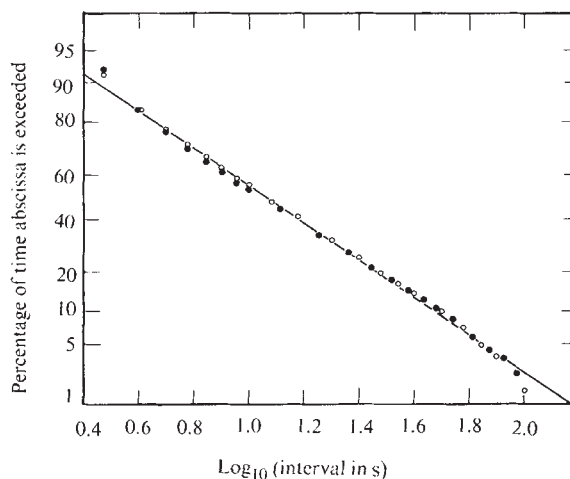


Fig. 2 Time intervals between successive lightning flashes plotted separately for the periods February to September 1969 and January to July 1970.

To reduce the computer time required for the original selection of likely lightning strokes, the computer was instructed to skip forward ten data points after each stroke was found (for one of the photometers). This restriction (to intervals longer than 2 s) avoided the detection of the rapid variations of intensity within a "single stroke". Individual lightning strokes have typical mean durations of 200 to 500 ms (ref. 6). It has been found that the logarithm of the intervals between lightning flashes (as well as the logarithm of the duration of the flashes) within a given storm, or within any of a number of simultaneously occurring storms, are normally distributed^{6,7}. The data reported here correspond to those from one thousand storms distributed over 60° of latitude (at all longitudes) throughout most months of the year (1969 to 1970). It is apparent from Fig. 2—in which the time intervals between individual lightning flashes for the periods February to September 1969 and January to July 1970 are plotted—that these data also follow a lognormal distribution. The intervals for both periods belong to the same lognormal distribution with a median flash interval of 11.5 s and a standard deviation of 0.48 log₁₀ units.

This work was supported by NASA and the US Office of Naval Research. A detailed description of the experiment will be published later.

Received July 12, 1971.

- ¹ Vorpahl, J. A., Sparrow, J. G., and Ney, E. P., *Science*, **169**, 860 (1970).
- ² Schonland, B., *The Flight of Thunderbolts* (Clarendon Press, Oxford, 1964).
- ³ Ney, E. P., *Nature*, **183**, 451 (1959).
- ⁴ Markson, R., *Pure Appl. Geophys.*, **84**, 161 (1971).
- ⁵ Brooks, C. E. P., *Quart. J. Roy. Meteor. Soc.*, **60**, 153 (1934).
- ⁶ Lakshminarayan, K. N., *J. Sci. Indust. Res.*, **21D**, 228 (1962).
- ⁷ Dennis, A. S., *J. Atmos. Sci.*, **27**, 170 (1970).

Formation of New Connexions in Adult Rat Brains after Partial Deafferentation

P. D. WALL & M. D. EGGER

MRC Cerebral Functions Research Group, Department of Anatomy, University College, Gower Street, London WC1E 6BT

Mapping of the receptive fields of cells in the thalamus and cortex after section of the dorsal columns in the rat reveals evidence of functional reorganization in the central nervous system.

BRAIN damage in adult mammals may be followed by remarkable recovery or by a depressingly permanent defect. Any understanding of this sometime plasticity would be important not only for therapy but also for understanding how the central nervous system adjusts to its environment during development and learning. During experiments designed for a different purpose, we came across evidence that a group of cells which had been deprived of their major input began to respond to quite novel stimuli after a few days. In these experiments, the cell bodies of the normal major input had been destroyed. The one class of explanation which cannot be invoked is true regeneration in which cells had divided and replaced the destroyed cells. In the mammalian adult central nervous system (CNS) there is no evidence for nerve cells which are still capable of division, growth and differentiation: following destruction of nerve cells, non-neural elements divide and migrate into the region of damage, phagocytosing the wreckage and replacing it with an impenetrable scar. Even if the cell bodies are intact but their axons are severed, there is no evidence of successful regeneration of axons within the CNS.

Our experiments involved the dorsal columns, through which cutaneous sensory afferents travel from the hind limbs to terminate on cells of nucleus gracilis. From this nucleus, axons decussate and project to the ventral posterior nucleus of the thalamus (VPL). Similar projection systems pass from the forelimb by way of the cuneate nucleus and from the face through the trigeminal nucleus. Within this region of the thalamus, the entire contralateral body surface is represented in an exact somatotopic map (Fig. 1). Recent experiments have suggested that discriminative cutaneous sensation survives the destruction of the dorsal columns¹. One explanation for this lack of effect is that other systems converge onto the thalamic nucleus and transmit the necessary afferent information by alternative pathways. To test this hypothesis, experiments were in progress to examine the response of cells in VPL before and after part of the dorsal column-medial lemniscus system had been destroyed. Responses had been recorded in VPL immediately before and after section of thoracic dorsal columns in eleven rats, and after destruction of one nucleus

gracilis in eight rats. We suspected that the full potentiality of the cells might not be revealed immediately after deafferentation and therefore decided to leave the animals for various times after the lesion before examining the thalamus. We encountered the unexpected result that cells in VPL which normally respond to leg stimulation began to respond to arm stimuli some time after destruction of nucleus gracilis. We shall report elsewhere the effect of acute and chronic deafferentation on the response of VPL cells to leg and body stimulation. Here we concentrate on those cells whose receptive fields switched from leg to arm.

Recordings were made in seventy-seven adult rats, ASH-CSE strain, weighing 200–400 g, under urethane (25%) anaesthesia, 0.65 ml./100 g. The head was held in a stereotactic machine with the lambda vertically above the ear bars in which position the centre of VPL is A 4.5, L 3.0 and 5.0 mm below cortical surface. The nucleus is crescent shaped in cross section and extends 1.4 mm rostrocaudally and mediolaterally. Thalamic recordings were made with glass-covered platinum microelectrodes whose impedance was 600–800 kohms at 1,000 Hz. When marking of electrode sites was required, recording was first carried out with silver plated steel microelectrodes followed by electrolytic deposition of iron which was later located by the prussian blue reaction. Cortical unit recordings were made with glass microelectrodes filled with 3 M KCl with impedance of 2–4 M ohms. When latencies were required, electrical stimuli were applied to the cutaneous receptive field of the unit through intradermal 30 gauge needles. Chronic lesions of nucleus gracilis or dorsal columns were made in sterile conditions with the animal anaesthetized with 'Equithesin'. With the head fully flexed and the cisterna magna open, nucleus gracilis can be observed directly without further dissection. The nucleus was destroyed by repeated maceration with honed jeweller's forceps. At various times after this lesion, thalamus or cortex was mapped and then the extent of the lesion was determined from serial frozen sections stained with darrow red-luxol fast blue. Only those animals with the lesion restricted to gracile nucleus are reported. In some, the extreme caudal end of the nucleus was spared.

Distribution of Receptive Fields

The distribution of receptive fields of cells in VPL was mapped in sixteen intact animals. In a further thirty-five animals maps were made of the intact VPL on one side so that these maps could be compared with those from the opposite VPL which had been partially deafferented by nucleus gracilis destruction. Successive recording points were distributed in a regular grid separated by 100 μ m vertically and 200 or 250 μ m

rostrocaudally and mediolaterally. For each station on this three dimensional grid, the entire body surface was brushed with medium pressure and the position was noted of any area of skin which evoked unit responses with an amplitude greater than 50 μ V.

In the normal VPL individual cells had small discrete receptive fields. Neighbouring cells recorded at a single electrode site had overlapping receptive fields restricted to some small area of the contralateral body surface. In 35% of the recording sites, cells responded to stimulation of trunk or proximal portions of the limbs or tail and these cells lie in the dorsolateral part of the nucleus. Twenty-four per cent responded to lower hind leg or feet or toes and lie ventrolaterally. Forty-one per cent responded to lower forearm or hands or fingers and are located ventromedially. The ventral surface of the nucleus is made up of a lamina about 200–400 μ m thick which contains cells that respond to passive movement of the limbs. Ventral to the arm area these cells respond to arm movements and the cutaneous leg zone has leg movement cells ventral to it.

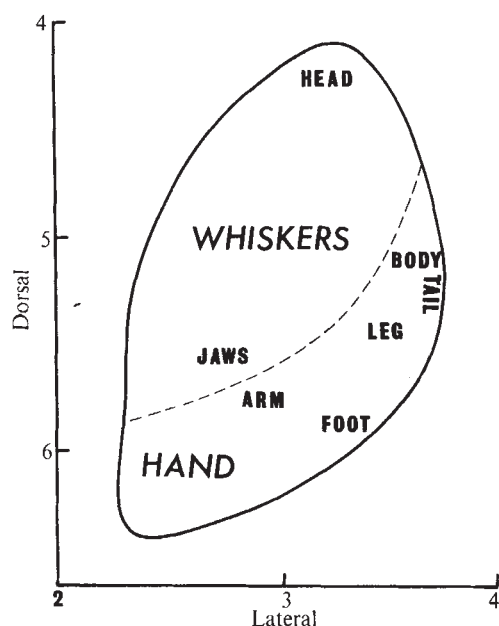


Fig. 1 Diagram of the representation in rat thalamus of the contralateral body surface. The region in which arm, trunk, leg and tail is represented in nucleus ventralis-posterior-lateralis. Maps are produced by placing microelectrodes successively at many locations in a single transverse plane in the region. For each recording point, the face and body surface is mechanically stimulated. Cells close to the recording electrode respond to a small area of skin. A combination of the receptive fields for all the points provides a map of the entire skin surface. The transverse plane is 4.5 mm rostral to external auditory meatus and the areas show distances in mm lateral to the midline and vertically below the cortical surface.

Cross-sectional maps were made first of one side and then continued across the midline to investigate the opposite nucleus. Fifty-seven pairs of maps were made in twenty animals at various stages after destruction of *n. gracilis*. Five variables were compared in the normal nucleus and its partner which had lost afferents: (1) the stereotactic coordinates of areas responding to particular parts of the body; (2) the ratio of the number of points on each side which responded to certain stimulus sites; (3) the monopoly by hind limb cells of the rostral pole of the normal nucleus; (4) the map in the ventral lamina of movement detection cells, which was unaffected by *gracilis* lesions and therefore provided another marker; (5) the receptive fields and latencies of selected single cells.

In rats mapped 1 or 2 days after destruction of the *n. gracilis* the picture is the same as immediately after the lesion (Fig. 2).

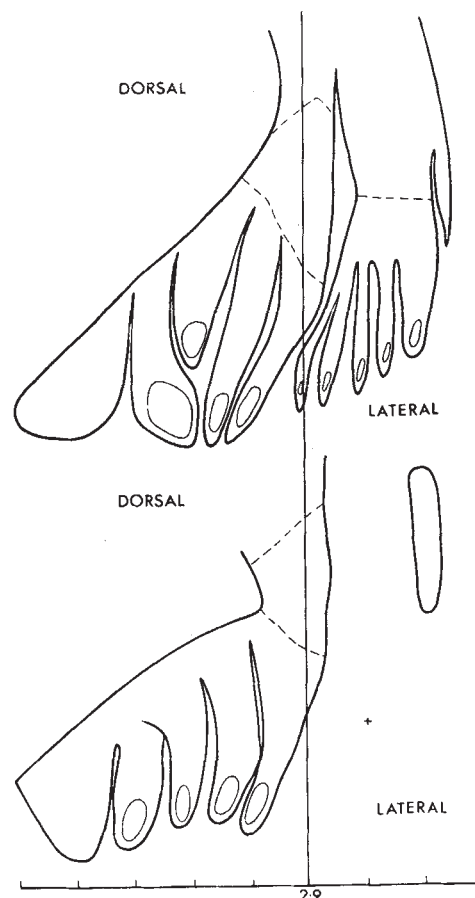


Fig. 2 Transverse map of distribution of receptive fields in VPL in rat 1 day after destruction of nucleus gracilis on one side. The map above shows the distribution in the thalamus supplied by the intact dorsal column nuclei with the forelimb representation medial, leg lateral, and body dorsolateral. The dotted lines mark the elbow and wrist on arm and the ankle on leg. The face area is not mapped. The map below shows the result of continuing the transverse search plane directly across the midline to the opposite thalamus which is not receiving an input from nucleus gracilis. The arm-hand-finger area is very similar in both maps. The leg area contained no responding cells in this plane with one exception marked by a cross. The horizontal axis marks 200 μ m intervals in the mediolateral direction. The vertical line marks electrode tracks 2.9 mm from the midline penetrating both left and right thalamic maps. These tracks passed through the lateral arm region in each thalamus and show how similar the two arm regions are.

The lower arm-hand-finger area is unchanged. In the leg-foot-toe region, there is an almost complete disappearance of sites where stimuli evoked activity. We shall describe the nature of these scattered responses to leg stimuli and those in the body region in another paper. In eight of nine animals mapped 3–17 weeks after the lesion, responses to stimuli on trunk, tail and hind leg remained essentially the same as in the acute and short survival animals but there was an expansion of the arm area into regions normally responding to leg stimuli. Sites responding to body and proximal limb stimuli averaged 25% fewer than normal, those for leg averaged 87.5% fewer but the number of arm points increased by 24%. Examination of the maps in detail shows that this expansion is produced by a lateral movement of the lateral edge while the medial part remains unchanged (Fig. 3). This lateral zone subserves the lower arm and wrist and these sites increased by an average of 132%. The change was most marked at the rostral pole where the zone normally monopolized by leg cells was now occupied by arm cells. Arm cells now lay dorsal to cells which responded to leg movement. The 16 and 17 week survival animals showed no greater expansion than the 3 week survivors. In no animal

was the entire area which normally responded to hind limb invaded by the forelimb area. In a ninth animal with 3 week survival there were signs of expansion of the body area.

Time Course and Nature of the Change

The simplest explanation for the expansion would be the shrinking of deafferented cells with a simple moving over of the neighbours. In this case there would be no new connexions and the cortical somatotopic map would not be distorted. Successful maps were completed of the arm and leg area of main sensory-motor cortex on both sides in animals 2, 5 and 6 weeks after destruction of one *n. gracilis*. The animals were anaesthetized with urethane and the body surface stimulated as in the thalamic recording experiments. In order to obtain a sufficiently detailed map it was necessary to record the receptive fields of cortical units by penetrating 500 μ m into cortex with glass, 2–4 Mohms, KCl filled microelectrodes. Maps were constructed from a grid of recording points separated by 500 μ m. In all three animals, the arm area had expanded into the leg area and it must therefore be concluded that thalamic cells projecting to cortex had changed their peripheral receptive fields.

The simplest explanation for the appearance of new receptive fields would be that the deafferentation had unmasked existing afferents which are normally inhibited. This is unlikely because in this type of preparation even massive electrical stimuli to arm in the intact animal fail to excite cells with discrete receptive fields on leg. Furthermore, there is a time delay in the switching of receptive fields. During this period when the former leg cells fail to respond to peripheral stimuli, ongoing activity continues in them at at least the frequency of normally connected cells showing that the deafferented cells themselves do not go through a period of lowered excitability.

To postulate the formation of new connexions, it is necessary first to discover the time course of their development. Eleven animals were examined 1–7 days after the lesion. At 1 and 2 days there was no significant change. At 3 days, two of three animals showed some expansion but without invasion of the rostral pole. At 4 days one animal showed both expansion and rostral invasion while a second showed no change. Of two animals at 5 days, one showed the full picture of expansion and the other some expansion. A 6-day survivor was inconclusive but the 7-day animal showed the same full picture as those examined after 3 weeks. We conclude that the changeover begins at 3 days and is fully established between 1 and 3 weeks. The cell bodies of the changed cells lay 200–400 μ m from the original boundary of the normal area but one must remember that the dendrites of the innervated and deafferented cells might be intermingled so that any shift of connexion might be over very small distances.

It is conceivable that the stimulus for the change of connectivity is not the degeneration of the terminals but the absence of the normal afferent impulses which bombard the thalamic cells. This possibility was ruled out by sectioning the dorsal columns just caudal to *n. gracilis* leaving the nucleus itself intact. The section of the fibres was made to spare the more lateral component of dorsal columns which supplies the cuneate nucleus. Thalamic maps from this animal taken 7 days after the lesion showed no signs of expansion of the arm area into the silent region which no longer responded to leg stimuli. It is true that the thalamus would still be bombarded by the ongoing activity of the deafferented nucleus gracilis but this is presumably slight by comparison with that transmitted in the normal freely moving animal.

A possible explanation for the newly effective connexion is that a background of ineffective fibres from the cuneate nucleus lie scattered through the area normally innervated by *n. gracilis* and that these fibres mature and successfully stimulate the cells vacated by degenerating axons. The change could be either presynaptic or postsynaptic. If such a diffuse system of fibres existed, one might expect the receptive fields of the newly

connected cells to differ from those in the established part of the nucleus. In fact we were unable to differentiate the receptive fields of cells in the presumably newly invaded region from those medial to them either in terms of field size or threshold. It is a particularly suitable region for examining receptive fields because many cells respond to movement of one or more of the long whisker-like hairs protruding from the rat's volar wrist. Cells with precisely this type of receptive field seemed to be duplicated in the new territory. Another possible mechanism

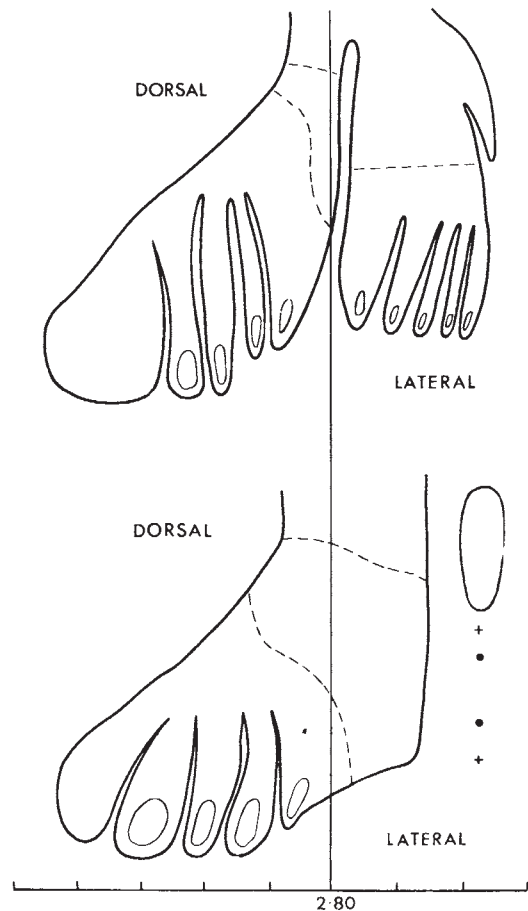


Fig. 3 Transverse map of distribution of receptive fields in intact VPL (above) and the map produced by continuing the mapping plane across the midline into the opposite VPL studied 7 weeks after destruction of the *n. gracilis* which projected to this nucleus (below). The vertical line marks an electrode track 2.8 mm from the midline which samples a similar region of the thalamus on the intact side to the vertical line shown in Fig. 2. The thalamus on the medial side of the line contains a similar map on both the intact and deafferented side. But the region representing the arm, especially the lower arm, has expanded on the operated side to invade a region which responds to leg on the intact side. At the lateral edge of the nucleus four cells were encountered which responded to body or leg stimulation but most cells in this region failed to respond to any peripheral stimuli.

is that the cells respond to an indirect input perhaps by way of cortex rather than by way of axons originating in cuneate nucleus. This seems unlikely because the latency of response of the switched cells was identical to that in the unchanged zone.

Collateral Sprouting

Probably the most likely explanation is that sprouts have grown from the terminal arborization of intact axons from cuneate nucleus and have established successful contact with

deafferented neighbours. Collateral sprouting and new contact formation have been shown to occur in the periphery both in denervated muscle² and in sympathetic ganglia³. In the central nervous system, light microscope evidence of sprouting into denervated regions has been provided for dorsal root fibres⁴ and for optic nerve fibres⁵. Raisman⁶ has shown clear electron microscope evidence for sprouting and end knob formation in the partially denervated septal nuclei of adult rat. But in the case of collateral sprouting, one must still explain the small receptive fields of the newly connected cells. The distance over which the sprouts would have to extend is not known, because although the cell bodies of the switched cells can be as much as 400 μm from the intact area it may be that the dendritic fields of the denervated cells overlap with those of the intact cells. If a sprout had only to grow a few μm to occupy a new cell, a pioneer sprout might lay down a pathway along which its neighbours could grow. Another way in which a restricted receptive field might be formed would be if the fibres which fire together grow together. This would require a mechanism by which the presence of more or less coincident impulse traffic in terminals would exaggerate the growth of terminals which sensed impulses in themselves and their neighbours.

Clearly an explanation of the phenomenon reported here will have to await an electron microscope examination of morpho-

logical changes in the region of changed response. In assessing the significance of the phenomenon of new connexions, one must give certain warnings. These observations were made in the rat, an animal which continues to grow throughout adult life, perhaps therefore retaining certain embryological characteristics. The distance over which new connexions could be established is evidently limited since there were no signs of occupation of vacant cells in the lateral edge of the nucleus. The new connexions do not represent recovery from the original lesions because information from arms is now channelled into a system presumably specialized to handle leg information. However, one might speculate that if scattered single cells were destroyed, as in an encephalitis, sprouting from associated collaborating neighbours might provide some functional advantage.

Received April 8; revised July 30, 1971.

¹ Wall, P. D., *Brain*, **93**, 505 (1970).

² Edds, jun., Mac V., *Quart. Rev. Biol.*, **28**, 260 (1953).

³ Guth, L., and Bernstein, J., *J. Exp. Neurol.*, **4**, 59 (1961).

⁴ Liu, C. N., and Chambers, W. W., *Arch. Neurol.*, **79**, 46 (1958).

⁵ Goodman, D. C., and Horel, J. A., *J. Comp. Neurol.*, **127**, 71 (1966).

⁶ Raisman, G., *Brain. Res.*, **14**, 25 (1969).

Temperature Changes associated with Adiabatic Decompression in Geological Processes

D. R. WALDBAUM

Department of Geological and Geophysical Sciences, Princeton University

Joule-Thomson coefficients of crystals indicate that temperatures may increase during irreversible adiabatic release of pressure. Isenthalpic decompression provides a mechanism for "self-heating" in igneous and metamorphic processes.

WHEN a substance is forced through a constriction in adiabatic conditions, the decompression is thermodynamically irreversible, occurring at constant enthalpy, H . For a normal fluid, the result may be either an increase or decrease in its temperature according to the initial and final pressures of the process¹⁻³. Joule and Thomson¹ showed that the effect may be measured directly or calculated from the relation

$$\left(\frac{\partial T}{\partial P}\right)_H = \frac{V(T\alpha_P - 1)}{C_P}$$

where T is thermodynamic temperature, P is pressure, α_P is isobaric thermal expansion $(1/V)(\partial V/\partial T)_P$, V is volume at P and T , and C_P is isobaric heat capacity.

This paper is concerned with the isenthalpic decompression coefficients (Joule-Thomson coefficients) of minerals, and their application to geological processes.

Decompression Coefficients of Crystals

For a crystalline phase, isenthalpic decompression produces an increase in its temperature inasmuch as $T\alpha_P \ll 1$. Table 1 lists values of $(\partial T/\partial P)_H$ at 1,000° C and 1 atm for minerals of basaltic and ultramafic rocks calculated from physical property measurements⁴. The sign and magnitude of the isenthalpic coefficients indicate that the temperature of a rock consisting of these minerals will change by approximately +220° C if the rock is decompressed across a pressure difference of 10 kbar by a strictly isenthalpic process, whether it be by extrusion or by some other mechanism.

For example, peridotite (or pyrolite) extruded from 20 kbar on an oceanic temperature-depth curve⁵ to 10 kbar would be heated sufficiently to intersect an experimentally determined "dry" solidus for basalt or peridotite^{6,7} (curve A, Fig. 1). Extrusion experiments by Bridgman⁸ on antimony metal, discussed in the present context by Adams⁹, suggest that a magma obtained by extrusion of crystalline rock might be ejected with nearly explosive force to still lower pressures, possibly to the surface.

It is relatively unimportant whether decompressed material melts or undergoes any phase changes. If decompression ends without a phase change, the heat exchanged between the decompressed material and its new surroundings may still cause anomalous heat flow at the surface¹⁰ and phase changes (metamorphism) in the surrounding rocks.

The process represented by the isenthalpic decompression curve *A* in Fig. 1 does not differ in principle from the assumption that magmas can form as a result of the rapid release of pressure from material, so that its temperature subsequently intersects a melting curve from the high pressure side^{11,12}. Such decompression requires at least a partially adiabatic process, otherwise the temperatures of the material would imitate those of the normal geothermal gradient. It is therefore usually implied that the pressure is released rapidly enough for the material moving upward to be always at a higher temperature than distant surrounding rocks at the same depth. But it is also assumed that the limiting maximum temperature in such a rapid release of pressure is that of an isentropic process^{7,12} (for example, curve *B*, Fig. 1). Fig. 1 illustrates quantitatively that all forms of adiabatic decompression of minerals do not necessarily lead to cooling.

Table 1 Adiabatic Decompression Coefficients of Some Minerals

Mineral	Formula	$(\partial T / \partial P)_H$ (°K/kbar)
Spinel	Mg ₂ AlO ₄	-21.0
Forsterite	Mg ₂ SiO ₄	-23.7
Fayalite	Fe ₂ SiO ₄	-23.0
Clinoenstatite	Mg ₂ Si ₂ O ₆	-21.0
Diopside	CaMgSi ₂ O ₆	-25.4
Jadeite	NaAlSi ₂ O ₆	-23.2
Albite	NaAlSi ₃ O ₈	-30.2
Anorthite	CaAl ₂ Si ₂ O ₈	-29.6
Magnetite	FeFe ₂ O ₄	-21.9
Chromite	MgCr ₂ O ₄	-23.0
Corundum	Al ₂ O ₃	-19.9
Periclase	MgO	-21.6
Rutile	TiO ₂	-24.8
Graphite	C	-23.4
Diamond	C	-13.4
α -Iron	Fe	-13.2
Nickel	Ni	-18.9
Platinum	Pt	-29.1

The isentropic coefficient $(\partial T / \partial P)_S$, or "adiabatic gradient", is $+1.0 \pm 0.5$ K/kbar for these substances. Pressure does not significantly affect the above isenthalpic coefficients in the range of Fig. 1. The effects of temperature are important, and will be discussed in a later paper; for silicates, the isenthalpic coefficients decrease by about 20% from 500° to 1,500° C. The effects of *P* and *T* are small enough that the above values serve as good estimates of the slopes of the true isenthalpic *P*, *T* curves from 800° to 1,200° C, in which case the line connecting the initial and final pressures of an irreversible decompression process is nearly coincident with the isenthalp itself.

It should not be inferred that a single stage isenthalpic process is required to produce heating. In any complex geological environment, when adiabatic decompression occurs, it is likely to consist of a series of isenthalpic and isentropic steps as shown by curve *C* in Fig. 1. A process involving only a small fraction of isenthalpic decompression steps could still result in an increase in temperature because

$$|(\partial T / \partial P)_H| \gg |(\partial T / \partial P)_S|$$

Recognizing that both isenthalpic and isentropic decompression represent limiting aspects of an adiabatic process, and that many other factors may affect the net result of pressure changes in geological processes, there are other geological situations where the isenthalpic contribution may be significant.

It is emphasized that the thermodynamic coefficients in Table 1, as with any thermodynamic property, may be applied to real or hypothetical processes whose physical mechanisms differ considerably in detail. It is not necessary to limit the application of isenthalpic decompression to conditions of high-velocity flow^{1,2,9}. The only condition to be met is conservation of enthalpy in the material undergoing decompression.

Flow Processes

Extrusion and throttling are examples of a large class of phenomena where a stationary flow is maintained in an isolated part of a mass bounded by streamlines, or through a tube of varying cross-section (as, for example, in the mantle convection model of Turcotte and Oxburgh¹³, although they assume an isentropic model). Enthalpy remains constant along such an adiabatically enclosed "tube" of flowing material^{3,14}. The isenthalpic coefficients of minerals indicate that the temperature of an isolated mass will rise during decompression and flow, even in the idealized case where friction, viscosity, and turbulence are ignored.

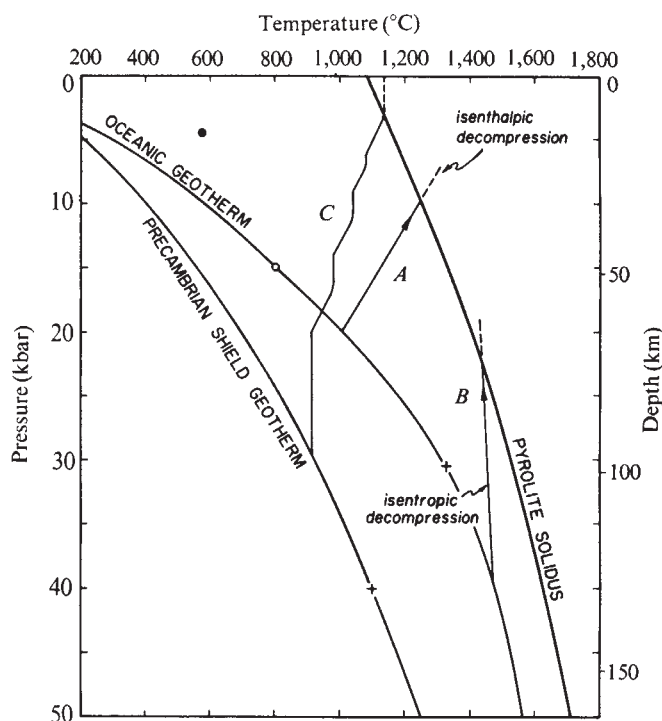


Fig. 1 Diagram comparing isenthalpic decompression (*A*), isentropic decompression (*B*), and a composite decompression curve (*C*) for a rock consisting of silicate minerals in Table 1. Temperature-depth curves are taken from ref. 8; the curve representing beginning of melting of pyrolite III composition is taken from ref. 10. The decompression curves are extended as a dashed line beyond their intersection with the melting curve, due to possible complications and uncertainties in the enthalpies of fusion, physical properties of the fluid, and the rate of migration of the fluid from the point of extrusion. Open circle denotes minimum depth from which decompression could cause a rock of pyrolite composition to begin melting in the absence of water. Small dot represents andalusite-kyanite-sillimanite triple point. Crosses indicate approximate depths from which forsterite would have to be decompressed at constant *H* to form a liquid at or near the surface.

The sign and magnitude of the isenthalpic coefficients thus provide a possible quantitative thermodynamic basis for the close association often observed between deformation, regional metamorphism, and partial melting of sedimentary rocks^{15,16}. The values are such that the observed effects of regional metamorphism can be obtained without necessarily requiring the addition of energy from external sources such as magmatic intrusions, by fluid transfer¹⁷, or by frictional heating¹⁸. The effects of adiabatic decompression, however, are only likely to be of importance in those areas where evidence for forced flow can be demonstrated¹⁹. Dewey and Pankhurst¹⁶ summarized studies on the distribution of metamorphic temperatures in time and space in the final episode of the Caledonian orogeny. The form of the proposed geothermal curves and their variation in time are consistent with a possible origin by isenthalpic flow. Similar observations summarized by Niggli²⁰ and Wenk²¹ for

the last stage of orogenic activity in the Central Alps may also be interpreted in this way.

As with any extrusion process, the resultant increase in metamorphic grade from simple isenthalpic decompression will depend on the initial temperature and pressure, the pressure difference causing flow, and the energy required for phase changes within the rock mass. Models of regional metamorphism based on thermochemical fluid dynamics will probably yield more satisfactory results than those based on a simple heat conduction model for an igneous intrusion²².

Considering the emplacement of alpine-type ultramafic rocks from this viewpoint, the observations of Raleigh²³, Dickey²⁴, and others may be extended to include the possibility that some peridotites and dunites originated as "peridotized" serpentinites²⁵ (which later reserpentinized, in part). Serpentine has an isenthalpic decompression coefficient of 26° C per kbar of differential (hydrostatic) pressure at 500° C, and calculations based on thermodynamic data⁴ support the hypothesis of Carpenter and Phyfer²⁵. An isenthalpic decompression of 9 kbar of partially serpentinized peridotite (initially one part serpentine to one part olivine by volume at 550° C and 10 kbar) yields an anhydrous peridotite at 1 kbar and 670° C. This result includes the conservation of enthalpy in dehydrating serpentine to less hydrous or anhydrous phases during decompression.

Isenthalpic decompression may be a mechanism in the lunar interior where heat sources of sufficient magnitude have not yet been conclusively identified for producing magma²⁶. This mechanism may contribute significantly to the formation of subsurface magma associated with the impacts of large meteorites²⁷ that produce fractures through which solid material might extrude. This mechanism allows for the possibility of early or recent lunar volcanism in a way that does not conflict with the hypothesis that the interior of the Moon has been relatively cold since the early stages of its formation. A similar mechanism could account for the origin of subsurface-derived magmas associated with the Sudbury (Canada) complex²⁸ and other terrestrial structures²⁹ thought to have resulted from meteorite impacts.

Shock Decompression

Another possible isenthalpic decompression process is that which occurs during the passage of a shock wave in a solid, although it is sometimes assumed, by analogy with the behaviour of gases, that compression alone causes the heating. Shock compression and decompression are largely adiabatic and irreversible, so these processes may occur at constant enthalpy. For example, any of the silicates in Table 1 would cool from room temperature to near absolute zero with only 12 kbar of compression at constant H (if such a process occurs). Enthalpy is gained, however, in the transfer of kinetic energy to the solid, so that very low temperatures may never be reached, but any net temperature rise on compression will be small. Subsequent decompression of only 100 kbar would form the high temperature crystalline phases and vesicular glass observed in shock-wave experiments on anhydrous minerals³⁰. Igneous rocks associated with impact structures^{28,29} may thus originate from two possible isenthalpic processes: shock decompression acting on the surface rocks and extrusion leading to melting at depth.

Isenthalpic shock-decompression may also cause magma to form from crystalline rock *in situ* at depth in seismically-active zones. The shock pressures required for high residual temperatures may be much less than previously estimated^{29,31} if attributed to isenthalpic rather than isentropic decompression.

To summarize, the sign and magnitude of the coefficients in Table 1 indicate that any process leading to a completely or partially isenthalpic decompression of minerals can, at least in principle, lead to an increase in their temperature. The prevailing opinion that the adiabatic parts of geological processes are entirely isentropic (reversible) requires some reconsideration. They are also likely to be irreversible in part, in which case data such as those in Table 1 apply. It should be possible

to explore these hypotheses in decompression experiments³² by attempting to duplicate the textures and mineralogy found in some of the geological environments described here. Some use could be made of high-pressure mineral synthesis or rock-deformation experiments that terminated unexpectedly by rapid decompression. Detailed petrographic study of these "unsuccessful" run products should yield information on textural and kinetic aspects of decompression that cannot be predicted by thermodynamics alone.

I thank R. B. Hargraves, R. E. Openshaw, L. M. Cathles, and L. S. Hollister for comments on the manuscript.

Received December 23, 1970; revised April 28, 1971.

- ¹ Joule, J. P., and Thomson, W., *Phil. Trans. Roy. Soc.*, **144**, 321 (1854).
- ² Adams, L. H., *J. Geol.*, **32**, 191 (1924); Barton, jun., P. B., and Toulmin, P., *US Geol. Survey Prof. Paper* 424D, D-350 (1961).
- ³ Pippard, A. B., *The Elements of Classical Thermodynamics*, (Cambridge University Press, 1957).
- ⁴ Kelley, K. K., *US Bureau Mines Bull.*, 584 (1960); Skinner, B. J. *Geol. Soc. Amer. Mem.*, **97**, 75 (1966); Robie, R. A., and Waldbaum, D. R., *US Geol. Survey Bull.* 1259 (1968).
- ⁵ Ringwood, A. E., Boyd, F. R., and Macgregor, I. D., *Carnegie Inst. Wash. Yearbook*, **63**, 147 (1964).
- ⁶ Yoder, H. S., and Tilley, C. E., *J. Petrol.*, **3**, 342 (1962).
- ⁷ Green, D. H., and Ringwood, A. E., *Contr. Mineral. Petrol.*, **15**, 162 (1967).
- ⁸ Bridgman, P. W., *Phys. Rev.*, **9**, 138 (1917).
- ⁹ Adams, L. H., *J. Wash. Acad. Sci.*, **12**, 407 (1922).
- ¹⁰ Horai, K., and Uyeda, S., in *The Earth's Crust and Upper Mantle* (edit. by Hart, P. J.), *Geophys. Monog.* 13, 104 (Amer. Geophys. Union, Washington, DC, 1969); Morgan, W. J., *Nature*, **230**, 42 (1971).
- ¹¹ Bowen, N. L., *The Evolution of the Igneous Rocks*, 315 (Princeton University Press, 1928).
- ¹² Turner, F. J., and Verhoogen, J., *Igneous and Metamorphic Petrology*, second ed., 443 (McGraw-Hill, New York, 1960).
- ¹³ Turcotte, D. L., and Oxburgh, E. R., *J. Geophys. Res.*, **74**, 1458 (1969).
- ¹⁴ Liepmann, H. W., and Roshko, A., *Elements of Gasdynamics*, 47 (Wiley, New York, 1957).
- ¹⁵ Turner, F. J., *Evolution of the Metamorphic Rocks*, *Geol. Soc. Amer. Mem.* 30, 286 (1948); Ramsay, J. G., in *The British Caledonides* (edit. by Johnson, M. R. W., and Stewart, F. H.), 168 (Oliver and Boyd, London, 1963); Thompson, jun., J. B., Robinson, P., Clifford, T. N., and Trask, jun., N. J., in *Studies of Appalachian Geology: Northern and Maritime* (edit. by Zen, E., et. al.), 215 (Wiley, New York, 1968); Thompson, jun., J. B., and Norton, S., *ibid.*, 325; Spry, A., *Metamorphic Textures*, 253 (Pergamon, 1969).
- ¹⁶ Dewey, J. F., and Pankhurst, R. J., *Roy. Soc. Edinburgh Trans.*, **68**, 361 (1970).
- ¹⁷ Shimazu, Y., *J. Earth Sci. Nagoya Univ.*, **6**, 31 (1958); Shimazu, Y., *Jap. J. Geophys.*, **2**, 135 (1961).
- ¹⁸ Reitan, P. H., *Lithos*, **1**, 161 (1968); Reitan, P. H., *Lithos*, **1**, 268 (1968).
- ¹⁹ Haller, J., *Geol. Rundschau*, **45**, 159 (1956).
- ²⁰ Niggli, E., *Fortschr. Mineral.*, **47**, 16 (1970).
- ²¹ Wenk, E., *Fortschr. Mineral.*, **47**, 34 (1970).
- ²² Turner, F. J., *Metamorphic Petrology: Mineralogical and Field Aspects*, 377 (McGraw-Hill, New York, 1968).
- ²³ Raleigh, C. B., in P. J. Wyllie, *Ultramafic and Related Rocks*, 191 (Wiley, New York, 1967).
- ²⁴ Dickey, J., *Min. Soc. Amer. Spec. Paper No. 3*, 33 (1970).
- ²⁵ Carpenter, J. R., and Phyfer, D. W., *Geol. Soc. Amer. Abstracts with Programs*, **1**, Pt. 7, 261 (1969).
- ²⁶ Ringwood, A. E., *J. Geophys. Res.*, **75**, 6470 (1970); Wood, J. A., *J. Geophys. Res.*, **75**, 6507 (1970); Smith, J. V., Anderson, A. T., Newton, R. C., Olsen, E. J., and Wyllie, P. J., *J. Geol.*, **78**, 395 (1970); Turcotte, D. L., and Oxburgh, E. R., *J. Geophys. Res.*, **75**, 6549 (1970).
- ²⁷ Baldwin, R. B., *The Face of the Moon* (University of Chicago Press, 1949); Ronca, L. B., *Icarus*, **5**, 515 (1966); Mackin, J. H., *Bull. Geol. Soc. Amer.*, **80**, 742 (1969).
- ²⁸ Dietz, R. S., *J. Geol.*, **72**, 412 (1964); French, B. M., *Bull. Vulcanol.*, **34**, 466 (1971).
- ²⁹ French, B. M., and Short, N. M., *Shock Metamorphism of Natural Materials*, 43, 59, 219 (Mono Book Corp., Baltimore, 1968).
- ³⁰ Milton, D. J., and De Carli, P. S., *Science*, **140**, 670 (1963); Dobretsov, N. L., Deribas, A. A., and Maly, V. I., *Phys. Earth Planet. Interiors*, **3**, 352 (1970).
- ³¹ Ahrens, T. J., Petersen, C. F., and Rosenberg, J. T., *J. Geophys. Res.*, **74**, 2727 (1969).
- ³² Bridgman, P. W., *Studies in Large Plastic Flow and Fracture*, 174 (Harvard University Press, Cambridge, 1964); Pugh, H. L. D., and Low, A. H., *J. Inst. Metals*, **93**, 203 (1965).

LETTERS TO NATURE

PHYSICAL SCIENCES

Ehrenfest's Paradox

ATWATER's remarks^{1,2} on the relativistic rotating disk problem (Ehrenfest's paradox³) have elicited considerable response⁴⁻⁶ of a somewhat peripheral nature. Atwater concludes that recourse to experiment is highly desirable. Arzelies⁷, while questioning the existence of relativistic constraints, also agrees with this view. The purpose of this communication is to point out what one might expect to observe as a disk rotates and to develop the magnitude in a practical case.

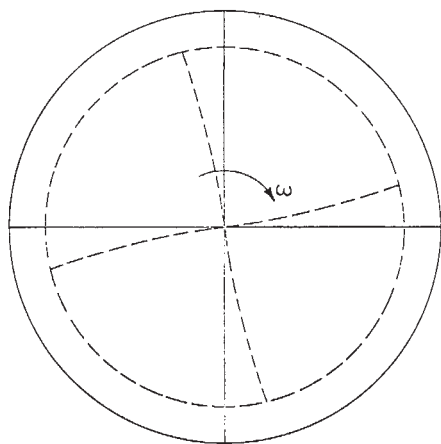


Fig. 1 A schematic representation of the rotating disk.

Suppose we have a disk of radius a rotating clockwise with angular velocity ω about an axis through its centre perpendicular to its plane. Take a radial element of the disk at distance r from the centre and consider a small section Δr along r . Then after one revolution, this section must have rotated counterclockwise with respect to its direction along r in consequence of the Thomas precession⁸.

It is easy to see that this angle (in radians) is given by

$$\delta\theta = \pi \frac{\omega^2 r^2}{c^2} \quad (1)$$

per revolution. Integrating along the whole element, we find it deflected counterclockwise by an angle

$$\theta = \frac{\pi}{3} \frac{\omega^2 a^2}{c^2} \quad (2)$$

per revolution.

Thus the appearance of the disk to a fixed observer will be as shown by the dotted lines in Fig. 1. It will be noted that the disk is in torsion with consequent reduction of both radius and circumference. Thus the premises leading to the Ehrenfest paradox need not exist. This description should

not be any more surprising than the well observed time dilation. A rotating disk is clock-like in character with the Thomas precession giving an accumulating measure of the number of revolutions. Further, the effect should be independent of the disk material, just as an equivalent clock is independent of its construction.

The relativistic constraints just introduced do, moreover, imply physical consequences for rotating bodies such as the Earth, pulsars, and so on, but this is considered elsewhere (D. H. W. and J. W. Kern, to be published). I wish to make clear that a practical laboratory experiment is entirely possible.

Take, for example, a disk 10 cm in diameter rotating 1,000 r.p.s. Then equation (2) yields $\theta \sim 10^{-12}$ per revolution. For a period of 30 days $\theta \sim 0.16^\circ$. This should be well within currently available means of measurement when the position of a point on the circumference is compared with a point near the axis.

This measurement might be conveniently carried out, for example, by placing a fiducial mark on the edge of the disk with a similar mark in the stationary frame adjacent to the edge. These marks can then be compared during rotation when illuminated by a discharge lamp triggered by a sharp magnetic pulse, or other means, positioned at a radial distance b on the disk. This will modify equation (2) and it then becomes

$$\theta = \frac{\pi \omega^2}{3 c^2} a^2 \left(1 - \frac{b^2}{a^2} \right) \quad (3)$$

per revolution.

With the passage of time, the mark on the disk will appear to move away from the fixed mark in accordance with equation (3) and counter to the direction of rotation.

D. H. WEINSTEIN

Superior Oil Company,
Houston, Texas, and
University of Houston,
Houston, Texas

Received June 14; revised July 23, 1971.

¹ Atwater, H. A., *Nature*, **228**, 272 (1970).

² Atwater, H. A., *Nature*, **230**, 197 (1971).

³ Ehrenfest, P., *Phys. Z.*, **10**, 918 (1909).

⁴ Suzuki, M., *Nature*, **230**, 13 (1971).

⁵ Marsh, G. E., *Nature*, **230**, 197 (1971).

⁶ Noonan, T. E., *Nature*, **230**, 197 (1971).

⁷ Arzelies, H., *Relativistic Kinematics*, 236 (Pergamon, London, 1966).

⁸ Thomas, L. H., *Nature*, **514**, 117 (1926).

Geomagnetic Dynamos in a Stable Core

Higgins and Kennedy¹ have suggested that the Earth's core is in stable equilibrium. If this is so there cannot be the large scale steady motions with a radial component which have

usually been thought necessary for the dynamo theory of the Earth's magnetic field. A stable fluid can have internal wave motions and it seems worth considering whether a body of fluid can act as a dynamo and produce steady electric currents and magnetic fields even when the motion is purely oscillatory. The work of Moffatt^{2,3}, Roberts⁴ and Steenbeck and Krause⁵ shows that this is so in an infinite fluid and it seems likely that it will be true in a sphere. The discussions of fluid dynamos are necessarily complex and we have therefore considered the very simple case of an oscillatory disk dynamo. This dynamo consists of a disk oscillating about its axis of symmetry with a coil connected to brushes on the axle and at the edge of the disk. Any current in the coil will produce a field, the motion of the disk in the field produces a current in the coil and maintains the field. The equation for the current, I , in such a system is easily shown to be⁶

$$L\dot{I} + RI = M\Omega I \quad (1)$$

where L and R are the inductance and resistance of the circuit, $2\pi M$ is the mutual inductance of the coil and the disk and Ω is the angular velocity of the disk. The equation bears an analogy to Maxwell's equations for the field, $\mathbf{B}$, in a fluid of conductivity σ and permeability μ moving with velocity $\mathbf{v}$, which give

$$\mathbf{B} - \nabla^2 \mathbf{B} / \mu \sigma = \text{curl} (\mathbf{v} \times \mathbf{B}) \quad (2)$$

In both cases the question is, can the interaction of the motion and the field, the term on the right, balance the second term on the left to give an average $\dot{I}$ or $\dot{\mathbf{B}}$ which is zero or positive? If the motion is oscillatory the answer will depend critically on the relative phase of the motion and the current or field, that is of Ω relative to I in equation (1) or $\mathbf{v}$ relative to $\mathbf{B}$ in equation (2) (the mean of $\cos t \sin t$ is zero, but the mean of $\cos^2 t$ is $\frac{1}{2}$). The study of equation (2) needs elaborate mathematical techniques, since $\mathbf{B}$ is a function of space as well as time. For equation (1), however, there exists an elementary solution; it shows that the phase relations are wrong and that the current is not maintained. It is known, for steady motion, that two coupled disk dynamos with the current from each feeding the coil of the other possess properties not shown by the single dynamo^{7,8}. We have studied such a system with oscillating disks and have shown that a current with a steady part may be maintained or caused to grow exponentially so long as some Fourier component of the oscillations of one disk is out of phase with the corresponding component of the motion of the other.

The simplest case is when each disk performs simple harmonic oscillations, the phase difference between the two being $\frac{1}{2}\pi$. The decay time of the current in the absence of motion is L/R , if this is large compared with the period of oscillation of the disks, then one coil has a steady current with a small ripple superposed and the other a much smaller alternating current. The calculations, which are very simple, suggest that dynamos with steady fields and oscillatory motions may exist in a wide variety of circumstances. Higgins and Kennedy, therefore, may not have seriously embarrassed the dynamo theory, even if their main contention is correct, as seems likely.

The detailed calculations will appear in a forthcoming book⁹.

E. BULLARD
D. GUBBINS

Department of Geodesy and Geophysics,
Cambridge CB3 0E2

Received July 15, 1971.

- ¹ Higgins, G., and Kennedy, G. C., *J. Geophys. Res.*, **76**, 1870 (1971).
- ² Moffatt, H. K., *J. Fluid Mech.*, **41**, 435 (1970).
- ³ Moffatt, H. K., *J. Fluid Mech.*, **44**, 705 (1970).
- ⁴ Roberts, G. O., *Phil. Trans. R. Soc.*, **266**, 535 (1970).
- ⁵ Steenbeck, M., and Krause, F., *Z. Naturf.*, **21a**, 1285 (1966).
- ⁶ Bullard, E. C., *Proc. Camb. Phil. Soc.*, **51**, 744 (1955).
- ⁷ Rikitaki, T., *Proc. Camb. Phil. Soc.*, **54**, 89 (1958).
- ⁸ Allan, D. W., *Proc. Camb. Phil. Soc.*, **58**, 671 (1962).
- ⁹ Bullard, E., and Gubbins, D. (in the press).

Variations in Magnetic Intensity and Climatic Changes

CORRELATION between the variations of the Earth's magnetic field, fluctuations in atmospheric radiocarbon activity, and climatic changes during the past 7,000 yr has been discussed extensively in the past¹⁻⁷. In addition, Harrison⁸ has suggested that reversals of the Earth's magnetic field could cause climatic changes. With an associate we have recently⁹ been able tentatively to conclude on the basis of studies of deep-sea sediment cores that in the past 470,000 yr the magnetism of the Earth has modulated climate. We have now extended the correlation between variations of the magnetic intensity and evidence of climatic change from deep-sea sediment cores back to 1.2 m.y.

Many investigators have studied remanent magnetism in deep-sea sediment cores¹⁰⁻¹⁵. The study was conducted according to the method of Opdyke *et al.*¹¹. The cores on which the remanent magnetism was measured were sampled at intervals of 2 to 10 cm and dried samples were cut into rough cubes measuring approximately 2 cm. Reversals were detected by finding the inclination of the remanent field of the series of samples with respect to the axis of the core. The samples were partially demagnetized in an alternating field of 150 oersted to remove unstable components.

Table 1 Details of the Cores that were Investigated

Core	Latitude (N)	Longitude (W)	Depth (m)	Length (cm)	Sedimentation rate (cm per 1,000 yr)
V12-122	17° 00'	74° 24'	2,800	1,090	2.32
V20-108	45° 27'	179° 14'	5,625	1,320	1.10
V26-41	19° 19'	26° 06'	4,340	1,400	1.16

The cores (Table 1) consist of a mixture of fine mineral particles and particles of calcium carbonate, except that core V20-108 contains no calcium carbonate.

Our climatic study is based on measurements of the abundance of the *Globorotalia menardii* group of planktonic foraminifera, including the four subspecies *G. menardii menardii*, *G. m. tumida*, *G. m. flexuosa* and *G. m. fimbriata*. Although Emiliani¹⁶, on the basis of a study by Lidz¹⁷, has maintained that the *G. menardii* group is unreliable as a climate indicator, we believe¹⁸ that Lidz's conclusion is misleading and that as a consequence, Emiliani's conclusion is ill-formulated. Therefore, like others¹⁹⁻²¹, we have taken the *G. menardii* group to be reliable for the study of climatic changes in most deep-sea sediment cores, with abundance indicating warm climate.

Fig. 1 shows correlation of the magnetic intensity curve of deep-sea sediment core V20-108 from the North Pacific, the *Globorotalia menardii* climate curve in core V26-41 from the North Atlantic, and the oxygen isotope climate curve of *Globigerinoides rubra* measured by van Donk²² in core V12-122 from the Caribbean. The magnetic intensity measurements in core V20-108 are according to Ninkovich *et al.*¹² and Foster²³ with adjustment for the stretched out top section. Because this core contains no calcium carbonate we cannot make foraminiferal measurements of the climatic changes. The time scales for cores V20-108 and V26-41 are based on magnetic reversals at the Matuyama-Brunhes boundary and at the Jaramillo event. The age for the Matuyama-Brunhes boundary is given by Cox and Dalrymple²⁴ who consider that the most probable age for this boundary is 0.69 m.y. The age and duration of the Jaramillo event is given by Opdyke²⁵ who places the upper boundary at 0.86 m.y. and the lower boundary at 0.92 m.y. with a duration of approximately 60,000 yr. The palaeomagnetic stratigraphy of core V20-108 was determined by Ninkovich *et al.*¹² and by Foster²³ and of

core V26-41 by Opdyke (personal communication). The time scale for core V12-122 was determined by Broecker and van Donk²⁶ based on thorium-230 dating by Ku and Broecker²⁷. It is in general agreement with the protactinium dating of the same core by Sackett²⁸.

Because the intensity measurements in core V20-108 are per gram of sediment and not per gram of magnetizable material in the samples, some of the variability in the intensity measurements in the core may be due to differences in composition and abundance of magnetic minerals in the sediment samples. Although the magnitude of the remanent magnetic moment in the core may be related to a change in the sedimentary sequences brought about by dilution of detrital components by biogenic components, it is difficult to imagine a scheme in which the direction⁹ of the recorded magnetic vector is changed systematically through depositional processes.

The changes in the sedimentary sequence in the North Pacific core, V20-108, which contains no calcium carbonate, could have been brought about by an influx of ice-rafted detritus which could have introduced a greater abundance of magnetic minerals in the cold periods. Therefore, we have plotted variations in magnetic intensity in this core against weight percentages of sediment coarser than 250 μm in particle diameter measured by Kent *et al.*²⁹. According to these authors this size fraction has been transported by icebergs.

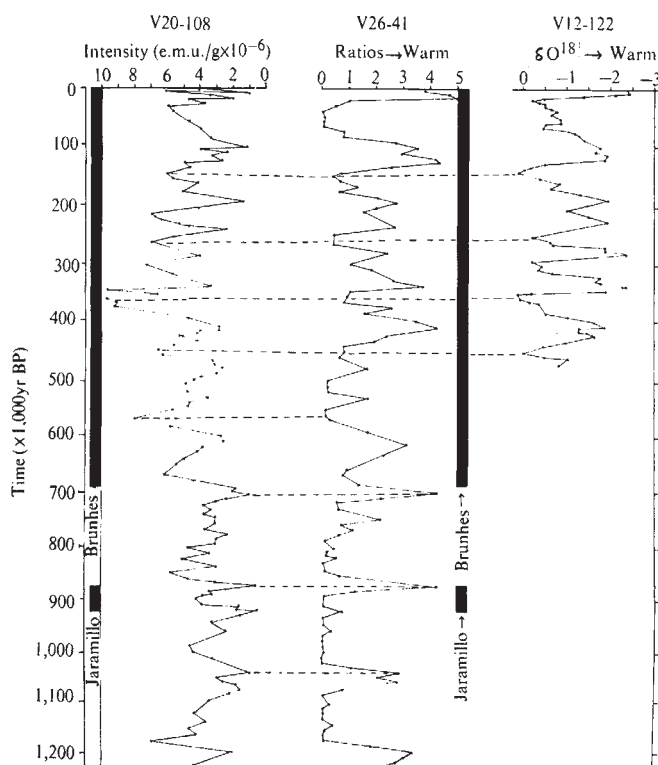


Fig. 1 Correlation of the magnetic intensity curve of deep-sea sediment core V20-108 from the North Pacific, the *Globorotalia menardii* climate curve in core V26-41 from the North Atlantic, and the oxygen isotope climate curve of *Globigerinoides rubra* measured by van Donk²² in core V12-122 from the Caribbean. The magnetic intensity measurements and the magnetic stratigraphy of core V20-108 are according to Ninkovich *et al.*¹² and Foster²³ with adjustment for the stretched out top section. Because this core contains no calcium carbonate we cannot make foraminiferal measurements of the climatic changes. The magnetic stratigraphy of core V26-41 was determined by Opdyke (private communication). The time scales for cores V20-108 and V26-41 are based on magnetic reversals at the Matuyama-Brunhes boundary and at the Jaramillo event according to dating of the boundary by Cox and Dalrymple²⁴ and dating of the event by Opdyke. The time scale for core V12-122 was determined by Broecker and van Donk²⁶ based on thorium-230 dating by Ku and Broecker²⁷.

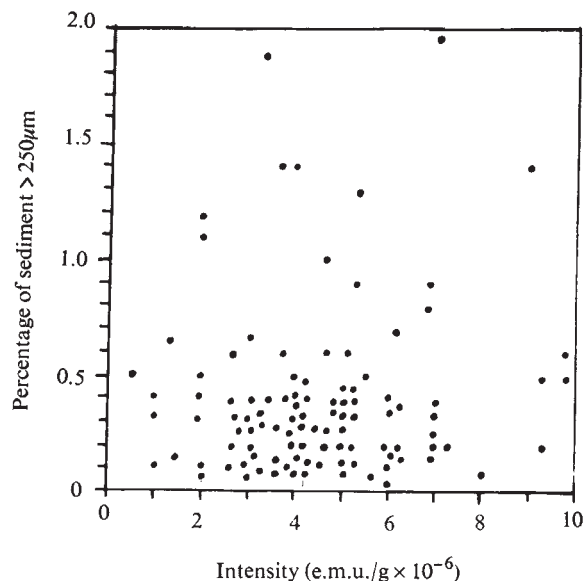


Fig. 2 Scatter plot showing that there is no correlation between magnetic intensity variations and changes in the sedimentary sequence in deep-sea sediment core V20-108 from the North Pacific. The changes in the sedimentary sequence could have been brought about by an influx of ice-rafted detritus which could have introduced a greater abundance of magnetic minerals in the cold periods. Therefore, we have plotted variations in magnetic intensity against weight percentages of sediment coarser than 250 μm in particle diameter measured by Kent *et al.*²⁹. According to these authors this size fraction has been transported by icebergs.

As Fig. 2 shows, there is no correlation between the magnetic intensity variations and changes in the sedimentary sequence.

On the basis of the results shown in Fig. 2 we suggest that the intensity measurements in core V20-108 may represent meaningful approximations of changes in the intensity of the Earth's magnetic field although we have not attempted to estimate the percentages of magnetizable material in the core.

We have shown correlations between variations in magnetic intensity and climatic changes. On the basis of evidence reported here and additional evidence⁹ we suggest that cause and effect relationship links changes of the Earth's magnetic field and climate. For instance, higher magnetic intensity seems to indicate colder climate. Thus we conclude that magnetism may modulate climate to some degree by the ability of the Earth's magnetic field somehow to provide a shield against solar corpuscular radiation.

We thank M. Ewing, J. Kukla, N. D. Opdyke, W. Pitman III, Bruce C. Heezen, J. van Donk, A. W. H. Be, D. Horn, J. H. Foster and B. Horn for help, and Janet Wollin and Julie McGowan for assistance in laboratory investigations. The research was supported by the US National Science Foundation.

GOESTA WOLLIN
DAVID B. ERICSON
WILLIAM B. F. RYAN

Lamont-Doherty Geological Observatory,
Columbia University,
Palisades,
New York 10964

Received May 28; revised July 2, 1971.

- ¹ Elsasser, W., Ney, E. P., and Winckler, J. R., *Nature*, **178**, 1226 (1956).
- ² Libby, W. F., in *Proc. Symp. Radioactive Dating and Methods of Low-Level Counting*, Monaco, March, 1967, 2 (International Atomic Energy Agency, Vienna, 1967).
- ³ Damon, P. E., in *Radiocarbon Variations and Absolute Chronology* (edit. by Olsson, I. U.) (Wiley Interscience, New York, 1968); *Met. Monog.*, **8**, 151 (1968).
- ⁴ DeVries, H., *Koninkl. Ned. Acad. Wetensch. Proc.*, **B61**, 94 (1958).

- ⁵ Bucha, V., Taylor, R. E., Berger, R., and Haury, E. W., *Science*, **168**, 111 (1970).
- ⁶ Suess, H. E., *J. Geophys. Res.*, **70**, 5937 (1965).
- ⁷ Suess, H. E., *Bild Wiss.*, **6**, 121 (1969).
- ⁸ Harrison, C. G. A., and Funnel, B. M., *Nature*, **204**, 566 (1964).
- ⁹ Wollin, G., Ericson, D. B., Ryan, W. B. F., and Foster, J. H., *Science* (in the press).
- ¹⁰ Harrison, C. G. A., and Funnel, B. M., *Nature*, **204**, 566 (1964).
- ¹¹ Opdyke, N. D., Glass, G., Hays, J. D., and Foster, J. H., *Science*, **154**, 349 (1966).
- ¹² Ninkovich, D., Opdyke, N. D., Heezen, B. C., and Foster, J. H., *Earth Planet. Sci. Lett.*, **1**, 146 (1966).
- ¹³ Glass, B., Ericson, D. B., Heezen, B. C., Opdyke, N. D., and Glass, J. A., *Nature*, **216**, 437 (1967).
- ¹⁴ Hays, J. D., Saito, T., Opdyke, N. D., and Burkle, L. H., *Bull. Geol. Soc. Amer.*, **80**, 1481 (1969).
- ¹⁵ Kennett, J. P., and Watkins, N. D., *Nature*, **227**, 930 (1970).
- ¹⁶ Emiliani, C., *Science*, **168**, 822 (1970).
- ¹⁷ Lidz, L., *Science*, **154**, 1448 (1966).
- ¹⁸ Wollin, G., Ericson, D. B., Ewing, M., in *Late Cenozoic Glacial Ages* (edit. by Turekian, K. K.), 199 (Yale University Press, 1971).
- ¹⁹ Imbrie, J., and Kipp, N. G., in *Late Cenozoic Glacial Ages* (edit. by Turekian, K. K.), 71 (Yale University Press, 1971).
- ²⁰ Beard, J. G., in *The Marine Quaternary of the Caribbean and Gulf of Mexico Regions*, SEPM Symposium, 535 (1969).
- ²¹ Schott, W., *Wiss. Ergebu. Deut. Atlant. Exped. Meteor.*, 1925-27, 3, 43 (1955).
- ²² van Donk, J. thesis, Columbia Univ. (1970).
- ²³ Foster, J. H., thesis, Columbia Univ. (1970).
- ²⁴ Cox, A., and Dalrymple, G. B., *Earth Planet. Sci. Lett.*, **3**, 173 (1967).
- ²⁵ Opdyke, N. D., in *The Application of Modern Physics to the Earth and Planetary Interiors* (edit. by Runcorn, S. K.), 549 (Wiley Interscience, London, 1969).
- ²⁶ Broecker, W. S., and van Donk, J., *Rev. Geophys. Space Phys.*, **8**, 169 (1970).
- ²⁷ Ku, T. L., and Broecker, W. S., *Science*, **151**, 48 (1966).
- ²⁸ Sackett, W. M., in *Symp. Marine Geochem.*, Graduate School of Oceanog. Univ. Rhode Island Occasional Pub. No. 3, 29 (1965).
- ²⁹ Kent, D., Opdyke, N. D., and Ewing, M. (in the press).

Spontaneous Fission of Heavy Transuranium Elements in the Surface Layers of the Peculiar A Star HR 465 explains Promethium Abundance

THE possibility that transuranium elements are present in the surface layers of peculiar A stars was raised last year^{1,2} after Jaschek and Malaroda³ announced evidence for the presence of uranium lines in the Ap star 73 Dra. Further information about the abundances of transbismuth elements in peculiar A stars is now available⁴⁻⁶ and there is strong evidence^{7,8} for the presence of promethium lines in the peculiar A star HR 465. All these facts imply, in the framework of the Guthrie-Van den Heuvel theory of the origin of Ap stars^{9,10}, that a search for transuranium elements in the spectra of those stars, at least in those in which uranium or promethium has been detected, should give positive results. It may even be possible to find the spectral lines of superheavy elements from the island of stability¹¹ near $Z=114$.

The implications resulting from the presence of uranium are self-explanatory^{1,2} whereas this is not so if promethium is present. We therefore present some qualitative arguments in favour of our hypothesis that the promethium which is observed in HR 465 is continually produced in the spontaneous fission of very heavy transuranium elements, possibly superheavy elements which have been sought for in numerous experiments.

The longest lived promethium isotopes, ¹⁴⁵Pm ($T_{1/2}=17.7$ yr) and ¹⁴⁶Pm ($T_{1/2}=5.55$ yr), are neutron-deficient and cannot be produced in any neutron capture chains. The other Pm isotopes which could have been produced in the r process have even shorter half-lives. It is thus unrealistic to attribute the promethium abundance in the Ap star HR 465 to fast neutron capture which occurred either in the primary star of

the binary system or in the surface of the recent peculiar star. The amount of promethium that should have been produced could not survive until now. We could think about some kind of continual production of promethium in surface reactions either with helions or with protons that might be accelerated in areas of high magnetic field density. This would be some *ad hoc* extension of previous concepts^{12,13} and it seems very improbable. From a detailed analysis of the various possible production modes of Pm (Kuchowicz, work in preparation) it seems that only spontaneous fission of very heavy nuclides provides a natural mechanism for this. This is because the two promethium isotopes ¹⁴⁷Pm and ¹⁴⁹Pm, with half-lives of 2.62 yr and 53.1 h, respectively, occur in isobaric decay chains of fission products. An interesting result from a recent analysis of the product yield curves for fission of various nuclei¹⁴ is that the total yield for the chains involving promethium is approximately constant (about 2% for $A=147$, and 1% for $A=149$) for light transuranium elements. For heavier elements, up to the additional island of stability near $Z=114$, it is expected that the light mass peak in the mass distribution of fission fragments is shifted towards the heavy peak, and symmetric fission occurs. This enhances the yield of isobaric chains including promethium, and it may be even as high as 5%.

We thus see that promethium cannot be regarded as a rare fission product of the heavier fissioning nuclei. Provided large amounts of such nuclei were produced in the exploding primary component of the binary system¹⁰ and then they were transferred to the surface of the recent Ap star, they are a continuous source of promethium. It is important to notice that all superheavy nuclides eventually decay to spontaneously fissioning nuclei, and thus a final result of their initial presence in any material is an enrichment of the fission products in that material. Thus Dakowski¹⁵ proposed that the symmetric fission of superheavy nuclei may account for the anomalies in the isotopic compositions of Xe and Kr in meteorites. It cannot be excluded that the overabundances of certain rare earths in the Ap stars of the main group may be attributed to a similar reason.

It is important to know the initial abundance of superheavy nuclei in the surface matter of Ap stars. The synthesis of these elements in the r process is well understood. Schramm and Fowler¹⁶ obtained recently an abundance of ~ 0.6 for the eight long-lived superheavy nuclei with half-lives exceeding 10^3 yr (on the scale with $\text{Si}=10^6$). Thus if we know the promethium abundance in HR 465, it will be possible, in principle, to calculate from it the concentration of the superheavy nuclei in the atmosphere (which may exceed by many orders of magnitude the concentration of Pm).

An important conclusion of our reasoning is that promethium may also be present in other peculiar A stars, especially in those where uranium has already been found. Its abundance should be correlated to the occurrence of r-process elements. This should be confirmed by observation. It may also be possible that superheavy elements can be found in at least some of the peculiar A stars in which promethium will be present. With these elements regarded as a continuous source for promethium, we can hope that they still exist in observable amounts. It is only the lack of knowledge of their optical spectra that makes us unable, at present, to make a search for their lines in the spectra of peculiar A stars. It may be expected that in the future this can be overcome, but even now the observation of promethium seems to confirm the existence of superheavy elements suggested on the basis of other data by Marinov *et al.*¹⁷ and by Bhandari *et al.*¹⁸.

B. KUCHOWICZ

Department of Radiochemistry and
Radiation Chemistry,
University of Warsaw

Received June 24, 1971.

- ¹ Kuchowicz, B., *Nature*, **227**, 156 (1970).
- ² Kuchowicz, B., *Bull. Acad. Pol. Sci. Sér. Math. Astron. Phys.*, **18**, 673 (1970).
- ³ Jaschek, M., and Malaroda, S., *Nature*, **225**, 246 (1970).
- ⁴ Brandi, E., and Jaschek, M., *Publ. Astron. Soc. Pacific*, **82**, 847 (1970).
- ⁵ Guthrie, B. N. G., *Observatory*, **89**, 224 (1969).
- ⁶ Dworetzky, M. M., *Astrophys. J. Lett.*, **156**, L101 (1969).
- ⁷ Aller, M. F., and Cowley, C. R., *Astrophys. J. Lett.*, **162**, L145 (1970).
- ⁸ Aller, M. F., *Sky and Telescope*, **41**, 220 (1971).
- ⁹ Van den Heuvel, E. P. J., *Bull. Astron. Inst. Netherlands*, **19**, 11 (1967).
- ¹⁰ Guthrie, B. N. G., *Publ. Roy. Observatory Edinburgh*, **6**, 145 (1968).
- ¹¹ Kuchowicz, B., in *Proc. Intern. Conf. Heavy Ion Physics*, Dubna, February 1971 (Joint Inst. Nucl. Res., Dubna, in the press).
- ¹² Burbidge, G. R., and Burbidge, E. M., *Astrophys. J. Suppl.*, **1**, 431 (1955).
- ¹³ Brancazio, P. J., and Cameron, A. G. W., *Canad. J. Phys.*, **45**, 3297 (1967).
- ¹⁴ Wahl, A. C., in *Proceedings of the Symposium on Physics and Chemistry of Fission*, Salzburg, 1965, **1** (IAEA, Vienna).
- ¹⁵ Dakowski, M., *Earth Planet. Sci. Lett.*, **6**, 152 (1969).
- ¹⁶ Schramm, D. N., and Fowler, W. A., *Nature*, **231**, 103 (1971).
- ¹⁷ Marinov, A., Batty, C. J., Kilvington, A. I., Newton, G. W. A., Robinson, V. J., and Hemingway, J. D., *Nature*, **229**, 464 (1971).
- ¹⁸ Bhandari, N., Bhat, S. G., Lal, D., Rajagopalan, G., Tamhane, A. S., and Venkatavaradan, V. S., *Nature*, **230**, 219 (1971).

Tungsten-181 and Other Short Lived Fission Products in Ground Level Air in North Germany and North Norway

SAMPLES of atmospheric dust have been collected for several years at 1.5 m above ground in Brunswick (52° 18' N, 10° 28' E) as part of an environmental radioactivity surveillance programme. Before analysis, each filter, made from 'Microsorban' (Delbag, Berlin) is ashed at 450° C. The content of fresh fission products in the samples is then measured in a 10 cm

by 10 cm NaI(Tl) well-type scintillation spectrometer. Later, the ashes of all filters exposed during half a month—containing dust from about 50,000 m³ of air—are combined and measured in a 45 cm³ well-type Ge(Li) detector with a multichannel analyser (ND 2200). The activity concentrations of various fission products and certain cosmogenic radionuclides are evaluated from the γ -spectra numerically. Since October 1970 a filter sample containing dust collected from about 300,000 m³ of air in Tromsø (Norway) is also analysed once a month. Within recent months fresh fission products were detected on three occasions.

First, 10 days after the eleventh nuclear test of the Chinese People's Republic (October 14, 1970) ¹³¹I was found in a rain sample, dated October 24–25, 1970. The concentration was 2 pCi/l.; during the following days, dust samples both from Brunswick and Tromsø contained ¹⁴⁰Ba + ¹⁴⁰La, ¹⁴⁷Nd and ²³⁷U. In Brunswick the concentrations were 1.8, 1.2 and 3 fCi/m³ $\pm$ 20%, respectively. The activity concentrations of some other radionuclides are listed in Tables 1 and 2. The increasing ratio ¹⁰³Ru/¹⁰⁶Ru from 0.1 in October 1970 to 1.0 in late March 1971 (Brunswick) implies that most of these Chinese fission products reached the surface layer through the stratosphere during the spring peak.

Second, dust samples collected between December 24, 1970, and January 2, 1971, in Tromsø, and between December 30, 1970, and January 2, 1971, in Brunswick contained ¹³¹I and, in very low concentrations, ¹³²Te and ¹⁴⁰Ba + ¹⁴⁰La, probably produced by the United States underground nuclear test, Nevada, December 16, 1970.

Third, between April 2 and 6, 1971, ¹⁴⁰Ba + ¹⁴⁰La was found in Brunswick; by Ge(Li) spectrometry of the combined ashes of the filters exposed between March 31, 1971, and April 16, 1971, in Brunswick, ¹⁸¹W was also detected with a mean activity concentration of 0.27 fCi/m³ $\pm$ 20% (for quantitative evaluation the Ta K X-ray peaks were used); before and after this time interval, no ¹⁸¹W was detectable. The filter exposed in Tromsø during the same month also contained ¹⁴⁰Ba + ¹⁴⁰La as well as ¹⁸¹W, the latter with a concentration of 0.38 fCi/m³ $\pm$ 20%.

Table 1 Activity Concentrations in Brunswick (fCi/m³)

Sampling period	⁹⁵ Zr	⁹⁵ Nb	¹⁰³ Ru	¹⁰⁶ Ru	¹³⁷ Cs	¹⁴¹ Ce	¹⁴⁴ Ce
30.10.70–12.11.70	—	—	2.3	7.5	1.2	1.8	12
30.12.70–1.2.71	3.2	5.0	2.4	5.1	1.1	1.2	8.8
1.2.71–1.3.71	9.5	15	6.5	8.4	1.8	3.6	16
1.3.71–15.3.71	15	26	10	13	2.5	5.1	23
15.3.71–31.3.71	21	36	13	13	1.9	6.5	23
31.3.71–16.4.71	30	55	16	17	2.4	8.7	35
16.4.71–30.4.71	70	130	33	46	6.6	15	81
30.4.71–17.5.71	63	120	28	44	5.9	12	78
17.5.71–1.6.71	46	90	18	35	4.5	8.1	69
1.6.71–11.6.71	100	200	38	84	11	15	150

Relative standard deviation = $\pm$ 5%

Table 2 Activity Concentrations in Tromsø (fCi/m³)

Sampling period	⁹⁵ Zr	⁹⁵ Nb	¹⁰³ Ru	¹⁰⁶ Ru	¹³⁷ Cs	¹⁴¹ Ce	¹⁴⁴ Ce
2.1.71–1.2.71	2.0	3.4	1.2	3.9	0.84	0.72	7.2
1.2.71–16.2.71	3.8	6.3	2.6	4.7	0.96	1.5	8.8
16.2.71–1.3.71	8.5	15	5.6	10	2.1	3.0	18
1.3.71–16.3.71	11	19	7.2	10	2.1	3.7	19
16.3.71–1.4.71	15	26	9.0	11	1.9	4.6	20
1.4.71–30.4.71	32	59	16	21	3.3	7.6	39
30.4.71–1.6.71	46	88	19	33	4.7	7.8	59

Relative standard deviation = $\pm$ 5%

In December 1968 tungsten-181 was found in ground level air in Italy¹, Finland² and the United Kingdom³, after an underground nuclear test carried out in Nevada on December 8, 1968. The origin of the small ¹⁸¹W contamination detected in early April this year in North Germany and North Norway is still unknown.

Newspapers reported two USSR underground tests on March 22, 1971, in Siberia and on March 23, 1971, in the western Ural Mountains. At that time there was a prevailing westerly wind between Central Europe and the Ural region. If there was any venting into the atmosphere nuclear debris must have been transferred at first in easterly directions. Some days later a high pressure system arose over eastern Europe and led easterly winds to North Germany in early April, the time at which fresh fission products arrived at Brunswick. So it cannot be excluded with certainty that these fission products as well as ¹⁸¹W stem from one of the above mentioned USSR underground tests.

W. KOLB

Physikalisch-Technische Bundesanstalt,
D-33 Braunschweig.

Received July 9, 1971.

¹ De Franceschi, L., Gentili, A., Gremigni, G., and Guidi, P., *Nature*, **224**, 571 (1969).

² Blomquist, L., and Asikainen, M., *Nature*, **225**, 59 (1970).

³ Cambray, R. S., Fisher, E. M., Brooks, W. L., and Peirson, D. H., *AERE-R 6212*.

Composition of Airborne Lead Particles

KNOWLEDGE of the composition of airborne particles and the reactions that take place in the atmosphere is important to the understanding of the fate of these particles. Lead compounds are present in a concentration of about 1% in the particulate and information about their composition would be especially helpful to people conducting experimental studies on the health effects of lead in air.

Their work further showed that the mass median diameter of airborne lead particulate is about 0.25 μ m (ref. 4).

In our study, airborne particulate lead compounds were physically identified by using an electron microprobe (an ARL type EMX modified to give an electron spot size of the order of 0.2 μ m). Samples were taken from a controlled environment, near and at a distance from a busy highway, and in a rural area.

Airborne particulate was collected on 0.45 μ m 'Millipore' membrane filters, which were dissolved in acetone and the particles were centrifuged out of the resulting solution. The particles were then mounted in a film of nitrocellulose on ultrapure polished beryllium substrates, coated with about 300 Å of carbon. Beryllium was chosen because it has very low white radiation and no line interference with the elements of interest. The thin film of carbon eliminated any reaction with lead bromides, but did not interfere with the analysis.

All the analytical work was based on analysis by ratios of elements rather than by absolute intensities. This was necessary both because of the small particle size and because of the time allotted for data acquisition. It was possible to pick out the various classes of compounds apparently present and then return to individual particles known to be this compound—or at least suspected to be this compound—and analyse them in more detail. Several particles from each class of compounds and each sample were analysed in detail in this way.

Samples of airborne particles were collected near to and about 400 yards from Eight Mile Road, a state highway on the northern edge of Detroit that carries about 100,000 cars each day. Samples were also taken in a rural area about 400 yards from a very lightly travelled roadway that is 15 miles from the nearest city (population 25,000). The samples taken near the highway and at 400 yards from the highway contained about 2.6% and 1.2% lead respectively. The rural sample contained a few tenths of a per cent lead.

Samples were also taken of automobile exhaust; these were collected in a black bag—a 4,000 foot³ plastic container filled with clean dry air. For the study, 300 feet³ of exhaust gas taken from an automobile operating on the seven-mode Federal Cycle was passed into the bag. The ten-fold dilution

Table 1 Sample Composition by Electron Microprobe

Sample	Percentage of total particles counted													
	PbCl ₂	PbBr ₂	PbBrCl	Pb(OH)Cl	Pb(OH)Br	(PbO) ₂ PbCl ₂	(PbO) ₂ PbBr ₂	(PbO) ₂ PbBrCl	PbCO ₃	Pb ₃ (PO ₄) ₂	PbO _x	(PbO) ₂ PbCO ₃	PbOPbSO ₄	PbSO ₄
Black bag														
Zero time	10.4	5.5	32.0	7.7	2.2	5.2	1.1	31.4	1.2	—	2.2	1.0	—	0.1
18 h	8.3	0.5	12.0	7.2	0.1	5.6	0.1	1.6	13.8	—	21.2	29.6	0.1	—
Eight Mile Road														
Near road	11.2	4.0	4.4	4.0	2.0	2.8	0.7	2.0	15.6	0.2	12.0	37.9	1.0	2.2
400 yards	10.5	0.7	0.6	8.8	1.1	5.6	0.3	0.6	14.6	0.3	25.0	21.3	4.6	6.0
Rural site														
	5.4	0.1	1.6	4.0	—	1.5	—	1.0	30.2	—	20.5	27.5	5.0	3.2

Hirschler *et al.*¹ have shown that the chief lead products exhausted from automobiles are lead halides and ammonium lead halides; lead chlorobromide is the principal component. The automobile is the principal source of airborne lead². The fate of these materials and the changes in chemical composition in the atmosphere have been poorly understood. Work done by the Stanford Research Institute, using electron and X-ray diffraction, showed that most of the lead compounds in the atmosphere were amorphous or present in such low concentrations that identification was nearly impossible³.

prevents condensation. Samples for analysis were taken immediately after automobile exhaust was discharged into the black bag and 18 h later. The particulate samples from the bag were about 25% lead. They had a size distribution similar to that found in atmospheric samples.

Table 1 shows the electron microprobe data for the samples. Individual sizes from 0 to 0.2, 0.2 to 0.6, 0.6 to 2, and greater than 2 μ m were examined. Because the composition distribution was so similar for all sizes, the sample data were averaged.

BIOLOGICAL SCIENCES

Effect of Inclusion of Cellulose in an "Atherogenic" Diet on the Blood Lipids of Children

SUNDARAVALLI *et al.*¹ have reported that increased plasma and liver cholesterol induced by cholesterol feeding in the rat could be largely counteracted by the concurrent feeding of 20% cellulose in the diet. We now report the results of similar investigations on humans.

Ten girls (10–12 yr) who volunteered for the study received (1) control diet (2) control diet with cholesterol (4 g/day) and (3) control diet with cholesterol (4 g/day) and cellulose (100 g/day) in the same order; thus each subject acted as her own control. Each diet was fed for a period of 10 days and the faeces were collected for analysis during the last 3 days. Blood samples were taken at the end of each period, and total and free cholesterol were estimated according to Wootton², total lipids by the method of Sperry³ and phospholipids by the method described by Oser⁴.

The composition of the control diet is given in Table 1. The diet provided 1,880 kcalories/day, of which 72% was from carbohydrates, 18% from fat and 10% from protein. Various recipes were prepared from the ingredients shown in Table 1. The cholesterol supplement given during the second and third period was dissolved in the fat by gentle warming and this mixture was used for all the cooking. Cellulose (microcrystalline cellulose, 'Avicel-PH', marketed by FMC Corporation, Marcus Hook, Pennsylvania) given as supplement, formed 20% of the diet; this was mixed with wheat flour-corn starch blend and made into *chapathies* (unleavened bread) which were offered to the subjects. This cellulose is of very fine particle size (>300 mesh) and could be easily incorporated in the diet without affecting the taste and acceptability.

Table 1 Composition of Control Diet

Ingredients of control diet	Daily quantities (g)
Corn starch	150
Wheat flour (80% extraction)	150
Sucrose	40
Groundnut oil	35
Skim milk powder	50
Vegetables	50
Tea leaves	6
Salt	15
Condiments	18

Table 2 Serum Lipids and Faecal Bile Acids of Experimental Children

Diet	Control	Control with cholesterol	Control with cholesterol and cellulose
Cholesterol (mg/100 ml.)			
Total	137.5 (127.1–148.0)	226.3 (184.8–255.1)	170.3 (152.1–190.2)
Free	45.9 (40.3–52.2)	63.1 (51.0–72.1)	44.4 (36.5–57.5)
Total lipids (g/100 ml.)	0.61 (0.56–0.64)	0.81 (0.75–0.84)	0.66 (0.59–0.69)
Phospholipids (mg/100 ml.)	184.9 (170.1–192.1)	244.3 (212.0–266.0)	203.3 (185.3–213.2)
Faecal bile acids (mg/day)	78.5 (71.0–82.8)	146.9 (133.8–162.1)	212.7 (192.1–231.6)

Values for serum lipids and faecal bile acids of the children are given in Table 2. The concentration of serum cholesterol of subjects on the control diet was 137.5 mg/100 ml.; approximately 33% of this was in the free form. Feeding of cholesterol

Examination of the data for exhaust gas from the black bag is very informative. At zero time, a significant percentage of the exhaust particles consists of PbBr_2 , PbBrCl , Pb(OH)Br , $(\text{PbO})_2\text{PbBr}_2$ and $(\text{PbO})_2\text{PbBrCl}$. Some intermediate halides might also be present up to concentrations of 10%. After 18 h, about 75% of the bromide is gone. About 30 to 40% of the chloride compounds also appear to have been lost. The products formed are lead carbonates, oxycarbonate, and oxides. Basic lead carbonate may be the actual product rather than the oxycarbonate. As water is easily lost from these compounds in the electron beam, however, the product identified is the oxycarbonate. It is estimated that the particles examined contained less than 1% of cations other than lead.

The loss of bromine was confirmed using X-ray fluorescence to measure the ratio of bromine to lead in the particulates in the black bag. The ratio rapidly decreased with time, with most of the loss occurring during the first hour.

When the composition in the black bag at 18 h is compared with the samples taken from the atmosphere, striking similarities are apparent. The sample taken near Eight Mile Road still contains significant quantities of bromide, although not as much as in the black bag at zero time. On the other hand, the sample taken away from the road contains almost no bromide and is very similar in composition to the black bag sample at 18 h. As in the black bag, the chief reaction products are lead carbonates, oxycarbonate and oxides. Because of the presence of SO_3 in the atmosphere and the use of phosphorus additives in some fuels, small amounts of lead phosphate and lead sulphate are also found.

The sample from the rural area shows clearly that very little lead halide remains. The more insoluble lead salts make up the bulk of the lead particulates.

The results of this study make it unnecessary to postulate photolysis of the lead compounds⁵ to account for the loss of halogen. Indeed the results from the black bag in the absence of light make this impossible. The clear parallel between the results from the black bag and the atmosphere strongly suggests that the mechanism is not photolytic.

In the black bag, the primary reaction appears to be a simple acid base reaction with carbonate or hydroxide ion displacing the bromide ion and, in some cases, the chloride ion from the lead halides initially exhausted. Oxidation, however, cannot be ruled out completely.

These results suggest that lead oxide, lead carbonate, basic lead carbonate or a mixture of these would be a good choice for experimental studies of the health effects of lead in the atmosphere.

GARY L. TER HAAR

Research and Development Department,
Ethyl Corporation,
Ferndale, Michigan

MICHAEL A. BAYARD

Research and Development Department,
Walter C. McCrone Associates, Inc.,
Chicago, Illinois

Received March 18; revised July 2, 1971.

¹ Hirschler, D. A., Gilbert, L. F., Lamb, F. W., and Niebyski, L. M., *Ind. Eng. Chem.*, **49**, 1131 (1957).

² Engle, R. E., Hammer, D. I., Horton, R. J. M., Lane, N. M., and Plumlee, L. A., *Environmental Lead and Public Health* (Environmental Protection Agency, Air Pollution Control Office, 1971).

³ Robinson, E., and Ludwig, E. L., *J. Air Poll. Control Assoc.*, **17**, 644 (1967).

⁴ Robinson, E., Ludwig, F. L., DeVries, J. E., and Hopkins, T. E., *Variations of Atmospheric Lead Concentration and Type with Particle Size* (Stanford Research Institute, 1963).

⁵ Pierrard, J. M., *Environ. Sci. Tech.*, **3**, 48 (1969).

(4 g/day) resulted in a significant increase in serum cholesterol to 226.3 mg/100 ml. There were concomitantly significant increases in serum lipids and phospholipids. Inclusion of cellulose to the extent of 20% of the diet resulted in a significant reduction in serum cholesterol, total lipids and phospholipids. The faecal excretion of bile acids (mg/day) increased from 78.5 to 146.9 when cholesterol was included in the diet. Inclusion of cellulose in the diet to the extent of 20% increased the bile acid excretion to 212.7.

Keys *et al.*⁵ reported that cellulose in the diet did not exert any beneficial effect on lowering of cholesterol. The present studies, however, have shown that cellulose at higher levels (20% of the diet) exerts a beneficial effect in lowering serum cholesterol in children, receiving a hypercholesterolaemic diet. Sundaravalli and Narayana Rao⁶ reported that inclusion of microcrystalline cellulose even to the extent of 20% did not significantly influence the utilization of nitrogen in young weanling rats. The paucity of information about the fibre content of human diets makes it difficult to relate the present studies to diets as eaten normally. A study by Hardinge, Chambers *et al.*⁷ showed that the fibre intake could vary widely over a period of years without adverse effects on the digestive tract. The amount of cellulose used in these studies is certainly higher than commonly ingested in so called civilized diets.

The mechanism of the effect of cellulose is unknown, but it may result from increased excretion of bile acids in the faeces. Using tagged compounds, Portman and Murphy⁸ reported that inclusion of 20% cellufLOUR in a sucrose synthetic diet resulted in an increased excretion of cholate and degradation products of cholate.

We thank Dr H. A. B. Parpia for his interest.

K. S. SHURPALEKAR
T. R. DORAISWAMY
O. E. SUNDARAVALLI
M. NARAYANA RAO

*Applied Nutrition and Dietetics Discipline,
Central Food Technological Research Institute,
Mysore-2a*

Received March 19, 1971.

¹ Sundaravalli, O. E., Shurpalekar, K. S., and Narayana Rao, M., *J. Agric. Food Chem.*, **19**, 116 (1971).

² Wootton, I. D. P., *Micro-analysis in Medical Biochemistry*, fourth ed., 85 (Churchill, London, 1964).

³ Sperry, W. M., *Methods of Biochemical Analysis*, 2 (edit. by Glick, D.), 83 (Wiley, New York, 1955).

⁴ Oser, B. L., *Hawk's Physiological Chemistry*, fourteenth ed., 1060 (McGraw-Hill, New York, 1965).

⁵ Keys, A., Grande, F., and Anderson, J. T., *Proc. Soc. Exp. Biol. Med.*, **106**, 555 (1961).

⁶ Sundaravalli, O. E., and Narayana Rao, M., *J. Amer. Dietet. Assoc.*, **57**, 517 (1970).

⁷ Hardinge, M. G., Chambers, A. C., Crooks, H., and Stare, F. J., *Amer. J. Clin. Nutr.*, **6**, 523 (1958).

⁸ Portman, O. W., and Murphy, P., *Arch. Biochem. Biophys.*, **76**, 367 (1958).

Cytological Evidence for the Association of the Short Arms of the X and Y Chromosomes in the Human Male

EVIDENCE for the association of the X and Y chromosomes during the first meiotic division in man has been documented^{1,2}. Until the centromere positions of the meiotic chromosomes were located with certainty, no information about the arm relationship between the two sex chromosomes could be obtained. The identification of the positions of the centromere



Fig. 1 Cell in pachytene. The broken arrow points to a G group bivalent and solid arrow to an A group bivalent, most possibly chromosome number 2.

in human male meiotic chromosomes at the late diplotene stage has been reported³. This observation revealed that the short arm of the Y chromosome was in association with the short arm of the X chromosome. Partial support for this finding was presented by Pearson and Bobrow⁴, who interpreted fluorescent staining of the distal end of the long arm of the Y chromosome of the XY bivalent in man as evidence that the short arm of the Y chromosome was associated with the X chromosome. Because the centromere position of the X chromosome could not be demonstrated in their material, it was not possible to determine which arm of the X chromosome was associated with the short arm of the Y chromosome. The purpose of this communication is to provide additional cytological evidence for the association of the X and Y chromosomes at their short arms.

The technique for the preparation of the meiotic material was a modification of that reported previously⁵ and was as follows: after the outer membranous capsule (tunica albuginea) of the tissue was removed, the specimen was teased apart in a Petri dish containing 1% sodium citrate solution by the use of teasing needles. The Petri dish was agitated gently from time to time to loosen the maximum number of cells from the tubules. The cell suspension was decanted into a centrifuge tube and centrifuged at 1,000 r.p.m. for 10 min after which the supernatant was removed and 1 ml. of freshly prepared fixative (3:1 methanol and glacial acetic acid) was added in a dropwise fashion. The material was refrigerated at 4° C for 5 min, the cell button was then resuspended in fixative and placed in the refrigerator for a further 25 min. The cells were centrifuged and then washed in a new fixative until a button and a clear supernatant were obtained. The button of cells was then placed on clean slides, flame-dried and stained with Giemsa (Azure Blend Type, Harleco).

The materials used for this report were obtained from the testicular tissue of three men treated for cancer of the prostate. The dark staining bodies which we have taken to indicate the centromere positions were observed not only at the late diplotene stage³ but also at other stages of meiosis I. For example, some bivalents at pachytene could be readily identified on the basis of length and centromere positions (Fig. 1). It was still technically difficult, however, to identify all the individual bivalents at this stage, because they were elongated and intertwined. Convincing evidence that the dark staining region of the pachytene chromosomes was at the centromere position was presented by Fredga⁶ who karyotyped the pachytene chromosomes of the Wallaby kangaroo.

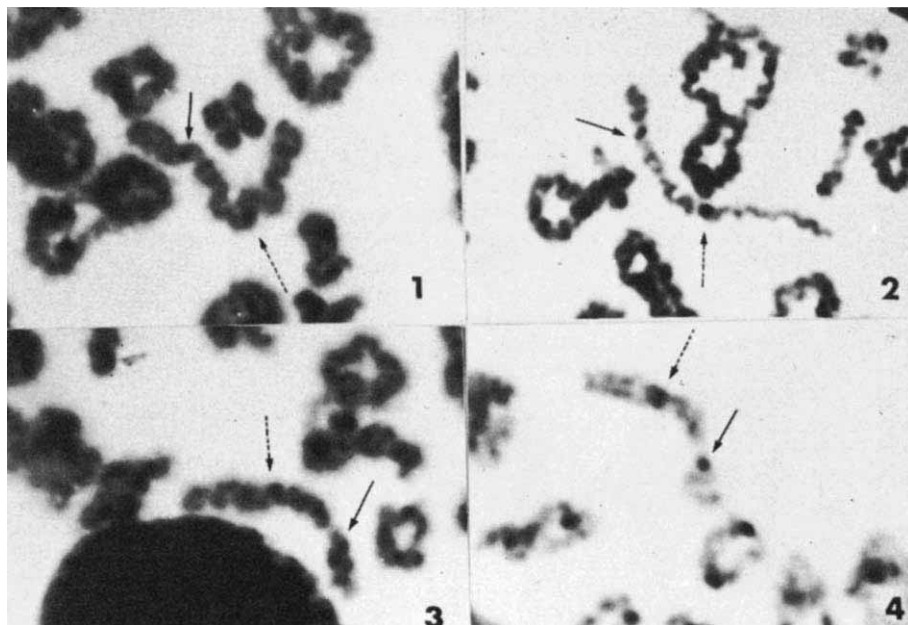


Fig. 2 Partial meiotic chromosome complement from four cells at or near diakinesis. The broken arrow points to the centromere position of the *X* chromosome and the solid arrow to that of the *Y* chromosome.

Although the arrangement of the *X* and *Y* chromosomes at pachytene could not be visualized because they were condensed into a heteropyknotic sex vesicle⁷, they were observed in an end to end relationship at the late diplotene stage as well as at diakinesis. The long and short arms of the two sex chromosomes from ten cells at the latter two stages were measured using camera lucida drawings. The measurements revealed that the mean ratio between the long and short arms of the *X* chromosomes was 1.37 (s.e.=0.05) and that of the *Y* chromosomes 3.57 (s.e.=0.18). Furthermore, the data confirmed the short arm association of the *X* and *Y* chromosomes (Fig. 2).

This study was supported in part by a grant from the Research Corporation. We thank Dr C. E. Ford for helpful comments.

ANDREW T. L. CHEN
ARTHUR FALEK

Division of Human Genetics,
Georgia Mental Health Institute
and Department of Psychiatry,
Emory University,
Atlanta,
Georgia 30306

Received August 24; revised December 7, 1970.

¹ Ford, C. E., and Hamerton, J. L., *Nature*, **178**, 1020 (1956).

² Hulten, M., Lindsten, J., Ming, P. M. L., and Fraccaro, M., *Ann. Human Genet.*, **30**, 119 (1966).

³ Chen, A. T. L., and Falek, A., *Science*, **166**, 1008 (1969).

⁴ Pearson, P. L., and Bobrow, M., *Nature*, **226**, 959 (1970).

⁵ Evans, E. P., Breckon, G., and Ford, C. E., *Cytogenetics*, **3**, 289 (1964).

⁶ Fredga, K., *Exp. Cell Res.*, **36**, 696 (1964).

⁷ Fraccaro, M., Hulten, M., and Lindsten, J., *Ann. NY Acad. Sci.*, **155**, 664 (1968).

Para-nucleolar Position of the Human *Y* Chromosome in Interphase Nuclei

INDIVIDUAL human chromosomes cannot be seen during interphase, and little is known of their intra-nuclear position during most of the cell cycle. The principal exception to this has been the *X* chromosomes: when there is more than one, they condense during interphase to form the sex chromatin, which is

often located on the nuclear membrane. It has recently become possible to locate the major portion of the *Y* chromosome in interphase nuclei¹, and we have used this technique to demonstrate that the *Y* chromosome is spatially associated with the nucleolus.

Because of their relatively large size and favourable morphology, cultured fibroblast nuclei were fixed in either methanol or Carnoy's fixative, stained with quinacrine¹, and viewed on a Leitz ortholux microscope fitted with Ploëm vertical illuminator. The use of incident ultraviolet light and transmitted white light facilitates fluorescent and phase contrast microscopic observations either simultaneously or in rapid succession. A comparison of photographs taken under phase contrast with the same nuclei after Giemsa staining confirmed that the nucleoli could be well defined under phase contrast.

Nuclei in which the *Y* body could be clearly identified were located, and then examined under phase contrast. Material was obtained from nine individuals of *XY* sex chromosome constitution, the mean number of cells scored per individual being 133 (range 59–256). The proportion of cells in which the fluorescent *Y* body was in contact with a nucleolus varied in different individuals from 37%–86%, the overall mean being 59.1%.

Ninety-four randomly selected cells were photographed, and the areas of nuclei and nucleoli measured by planimetry. The mean nucleolar area in different individuals ranged from a minimum of 8.92% (s.d. 3.7) to a maximum of 13.47% (s.d. 4.19) of the nuclear area. The overall mean for ninety-four cells was 10.7%. It is apparent that the proportion of cells in which the *Y* body lies in contact with a nucleolus considerably exceeds the expectation, had the *Y* body been randomly positioned within the nucleus. A similar association of the *Y* body with the nucleolus has also been observed in Sertoli cell nuclei, PHA-stimulated peripheral lymphocytes, and buccal mucosal cells, although phase-contrast observations are much more difficult to make on the latter cell types.

Fibroblast nuclei from a male of *XXX* sex chromosome constitution showed both *Y* bodies to be associated with the nucleolus in 36% of cells, while neither *Y* body was so associated in 24.6%. There was no tendency for both *Y*s to be associated with the same nucleolus. Nucleolar area was 11.98% (s.d. 2.95) of nuclear area.

In some species the number of nucleoli per nucleus can be related to the number of nucleolar-organizing regions present in the genome². We therefore investigated the relationship of

the number of *Y* chromosomes in the karyotype to the mean nucleolar count per cell. The within-individual variability of nucleolar counts made it difficult to get reproducible results on fibroblast nuclei, and this part of the investigation was therefore done on 72 h PHA-stimulated peripheral blood cultures. Preparations were stained with Giemsa, and the number of nucleoli counted in 100 consecutive cells. Two separate counts were made for each individual, and the results expressed as the mean number of nucleoli per nucleus (nucleolar index).

Table 1 Mean Number of Nucleoli per Cell (Nucleolar Index) in Cultured Lymphocytes of Different Chromosome Constitution

Group	Chromosome constitution	No. of individuals	Nucleolar index Mean	s.d.
1	46 XY	10	1.86	0.22
2	46 XX	10	1.68	0.29
3	47 XYY	4	1.77	0.21
4	47 XXY	3	1.74	0.16
5	45 XO	3	1.69	0.12
6	47 XXX	1	1.75	—
7	45 XY t(DqGq)	1	1.70	—
8	47 XX 13+	1	1.80	—
9	47 XY 21+	6	2.12	0.31
10	47 XX 21+	5	2.26	0.31

Data on forty-four individuals of different chromosome constitutions are summarized in Table 1. Analysis of variance on the whole data, and comparisons of group means with one another by *t* tests, demonstrated no significant effect of sex chromosome complement on the nucleolar index. Individuals with trisomy 21 had a significantly raised nucleolar index ($P < 0.001$ for both sexes combined). The numbers available for examination in some of the groups, however, are so small that real differences could have gone undetected.

Information on the nucleolus-organizing capacity of human chromosomes is based largely on the study of "satellite associations" persisting into metaphase. Although the *Y* chromosome long arm does have a secondary constriction³, and there have been suggestions that it may be involved in satellite association⁴, the weight of evidence seems to be against this view⁵. Our demonstration of a spatial proximity of this chromosome to the nucleolus does not necessarily imply a functional relationship, but several features of the *Y* chromosome may be relevant to this question. (a) Intense quinacrine fluorescence is characteristically seen, apart from the *Y* long arm, on the short arms of the acrocentric *D* and *G* group chromosomes and next to the centromere of chromosome 3. The *D* and *G* group short arms are the known nucleolus-organizing regions of the human genome⁶, and we have observed interphase fluorescence from a marker chromosome of this group associated with the nucleolus in a large proportion of nuclei. Whether the centromeric region of chromosome 3 is also related to the nucleolus is not yet known. (b) Recent techniques for demonstrating a form of constitutive heterochromatin stain the distal part of the *Y* long arms⁷. The procedure involves denaturing and reannealing DNA, and is thought to demonstrate highly repetitive DNA sequences. There is evidence that nucleolus-organizing regions consist of repetitive DNA⁸. (c) The intensely fluorescent part of the *Y* chromosome is known to vary considerably in size, and may even be completely absent, without apparent clinical effect^{9,10}. This is compatible with the concept that it is composed of genetic sequences also present elsewhere in the genome. (d) The only well proven function of the *Y* is in sex determination, and these genes are probably localized in the non-fluorescent area¹¹. (e) The human *Y* chromosome is relatively large compared with those of other primates, which lack intensely fluorescent chromatin¹². This again suggests a genetic content over and above that necessary for male sex determination.

These arguments are all indirect, but it seems possible that the distal part of the long arm of the *Y* chromosome contains a specialized form of genetic material related to nucleolar

function. Further investigation may throw light, not only on the function of the *Y* chromosome, but on the nature of the histochemical differentiation recently revealed within the human chromosome complement.

M. BOBROW
P. L. PEARSON
H. E. A. C. COLLACOTT

*MRC Population Genetics Unit,
Old Road,
Headington,
Oxford*

Received April 16, 1971.

- Pearson, P. L., Bobrow, M., and Vosa, C. G., *Nature*, **226**, 78 (1970).
- Busch, H., and Smetana, K., *The Nucleolus* (Academic Press, New York, 1970).
- Court Brown, W. M., *Human Population Cytogenetics* (North-Holland, Amsterdam, 1967).
- Gripenberg, U., *Chromosoma*, **15**, 618 (1964).
- Ferguson-Smith, M. A., and Handmaker, S. D., *Ann. Hum. Genet.*, **27**, 143 (1963).
- Ferguson-Smith, M. A., *Cytogenetics*, **3**, 124 (1964).
- Arrighi, F. E., and Hsu, T. C., *Cytogenetics* (in the press).
- Hsu, T. C., Brinkley, B. R., and Arrighi, F. E., *Chromosoma*, **23**, 137 (1967).
- Bobrow, M., Pearson, P. L., Pike, M. C., and El-Alfi, O. S., *Cytogenetics* (in the press).
- Borgaonkar, D. S., and Hollander, D. H., *Nature*, **230**, 52 (1971).
- Ferguson-Smith, M. A., *Bull. Europ. Soc. Hum. Genet.*, **4**, 39 (1970).
- Pearson, P. L., Bobrow, M., Vosa, C. G., and Barlow, P. W., *Nature*, **231**, 326 (1971).

Evidence for a Genetic Factor in the Transmission of Spontaneous Lymphosarcoma (Leukaemia) of Young Pigs

A HISTOLOGICAL SURVEY of lymphosarcoma¹ (leukaemia) in 1968 in abattoirs throughout Great Britain showed an incidence of twenty-five cases per million pigs slaughtered, that is, ninety-two cases from 3.7 million pigs. There was multicentric lymphosarcoma in fifty-seven pigs and thymic lymphosarcoma in thirty-five pigs, and there was no indication of lymphosarcoma in other pigs on the farms concerned or even that it had occurred there previously. It is therefore of some interest that we have now found lymphosarcoma to have occurred several times in a single herd.

A minimal disease (MD) piggery established in 1963 was stocked with colostrum-deprived hand reared Large White piglets obtained by caesarian section from nine unrelated sows. The herd has since been maintained as a closed community with fourteen to seventeen breeding sows and one or two boars. The only contact with other pigs has been the occasional use of semen from outside boars for artificial insemination.

In August 1966, lymphosarcoma was diagnosed in two 3 month old sibling piglets. These were the offspring of a boar (D) mated to his sister (362). The boar died before the mating could be repeated but the sister subsequently had litters of nine and four offspring respectively to another brother (138). None of these developed lymphosarcoma although four were kept for more than a year. No further cases were detected in the herd until September 1969, since when nineteen have occurred, all confirmed at necropsy as multicentric lymphosarcoma. Although present in many of these pigs, the thymus was not involved in the disease.

The age at which the disease could first be diagnosed with any certainty conformed to a more or less normal distribution between 6 and 18 weeks, apart from one case in which diagnosis was obscured for several weeks by intercurrent disease.

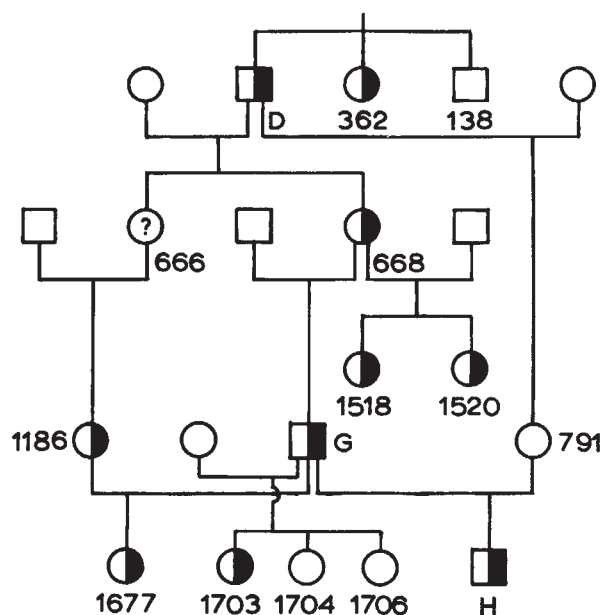


Fig. 1 Relationship between parents of lymphosarcoma cases; Square, male; circle, female; half filled symbol, parent of L/S; open symbol, not parent of L/S; ?, status doubtful, not suitably test-mated.

Most animals reared in the piggery are slaughtered for bacon at 5–6 months of age but to date eighty-two animals have been kept for breeding, most for 2 or 3 yr, some for 6 or 7 yr. No signs of lymphosarcoma have been detected in any of these which include all the parents of all known lymphosarcoma cases. The entity we are reporting is thus essentially a disease of young pigs. Occasionally we have found lymphosarcoma in older pigs in other herds but such cases are sporadic. This is in keeping with other reports^{1,3–5}.

Eleven of our cases were males (including five castrates) and ten were females. All resulted from matings with a degree of consanguinity of four or less between three boars and seven sows which had a common ancestry. The ways in which they were mated and the distribution of lymphosarcoma cases in the resultant litters are detailed in Table 1.

Table 1 Matings Producing Lymphosarcoma and Distribution of Cases among Litters

Boar	Sow	Matings Degree of consanguinity	Composition of litters		
			No lymphosarcoma Died before 6 weeks	At bacon weight (5–6 months)	L/S cases
D	362	2	2	7	2
G	668	1	3	7	1
			7	3	2
	1,186	4	1	9	1
			2	8	0
			6	6	2
	1,518	2	1	5	1
			1	9	1
	1,520	2	5	4	2
			4	9	2
	1,677	1	4	0	2
H	1,703	2	2	5	5

A number of piglets died before 6 weeks of age and are not included in our assessment of incidence of lymphosarcoma. This averaged 22.6% which is not significantly different from the 25% to be anticipated if an autosomal recessive gene were involved ($\chi^2=0.03$, 1 d.f.). This hypothesis is supported by the facts that when any of the ten parents of lymphosarcoma cases was mated to other pigs no cases were found among 478 offspring in fifty-seven litters, nor were any cases encountered in 753 offspring in ninety-nine litters arising from matings which excluded the ten, even though in both groups about a quarter of the matings had a degree of consanguinity of four or less.

A proportion of animals in the affected strain would be expected to be non-carriers of the disease. We have found four such animals (138, 791, 1,704, and 1,706). It has so far not proved possible to use affected animals in test matings which might help to confirm the hypothesis because they have all remained stunted and sexually immature even when living to be more than 1 yr old.

Evidence from Russia⁶ suggests that in cattle susceptibility to the disease is inherited through a recessive homozygous factor but the situation differs from ours in that the disease in cattle tends to appear later in life when they have already bred successfully and in the Russian herd every affected offspring had an affected or suspect parent.

We thank Professor Sir Alexander Robertson for encouragement and facilities.

H. S. McTAGGART
K. W. HEAD
A. H. LAING

Royal (Dick) School of Veterinary Studies,
University of Edinburgh,
Easter Bush,
Roslin,
Midlothian

Received April 5; revised May 17, 1971.

- Anderson, L. J., and Jarrett, W. F. H., *Cancer*, **22**, 398 (1968).
- McTaggart, H. S., and Rowntree, P. G. M., *Brit. Vet. J.*, **125**, 240 (1969).
- Meier, H., *Adv. Vet. Sci.*, **7**, 43 (1962).
- Cotchin, E., *Vet. Rec.*, **72**, 816 (1960).
- Monlux, A. W., Anderson, W. A., and Davis, C. L., *Amer. J. Vet. Res.*, **17**, 646 (1956).
- Emeljanov, A. S., Smolina, K. A., and Smetanina, G. K., *Zhivotnovodstvo, Mosk.*, **28**, 53 (1966).

Cell Division in Medium lacking Serum Growth Factor: Comparison of Lines transformed by Different Agents

CELLS of the permanent lines derived from mouse embryo tissue, 3T3 and Balb/c 3T3, exhibit density dependent inhibition of cell division^{1,2} anchorage dependence^{3,4}, and also require a factor in serum to initiate DNA synthesis^{5–8}, but these growth controls^{4,6,9–11} are lost in transformed cells. It has been suggested that loss of density dependent inhibition is a consequence of the loss of a requirement for serum factor⁶, in which case it would be expected that transformed lines derived from 3T3 would lack both growth controls. We have therefore tested various transformed lines of Balb/c 3T3 lacking the density dependent inhibition for the ability to grow without this serum factor or factors. Both virus-transformed lines of Balb/c 3T3 and independent isolates of Balb/c 3T12 (see ref. 2) grow well in medium lacking the serum growth factor(s), but most non-virus-transformed variants of Balb/c 3T3 grew poorly if at all. These observations suggest that the loss of density dependent inhibition of growth does not necessarily depend on the loss of the need for serum growth factor.

Balb/c 3T3, clone A31, was separately transformed by the small plaque mutant of SV40, the Kirstein and Moloney strains of murine sarcoma virus (MSV) and the Bratislava strain of Rous sarcoma virus (RSV). Most of the other transformed clones were isolated from the occasional cells that spontaneously grew out of the Balb/c 3T3 monolayer. We also used one transformed line induced by X-irradiation (1,500 rads) and another induced by ultraviolet light (2,000 ergs mm⁻²). All the transformed lines had saturation densities ranging from $3.5\text{--}7 \times 10^5$ cells cm². The preparation of factor-free medium which permits growth of SV40-transformed Balb/c 3T3 but not of normal cells has been described¹².

Exponentially growing cultures were trypsinized and planted in factor-free medium and medium containing 10% whole calf serum (complete medium) at cell concentrations ranging from 100–6,000 cells per 50 mm Petri dish (Falcon). After 2–3 weeks the plates were fixed, stained¹² and the colonies scored. In case the lines did not grow in factor-free medium because they were unable to settle onto the plastic dish, all lines with little or no growth were also planted in complete medium and changed to factor-free medium 1 day later.

Fig. 1 gives the relative plating efficiencies of cells in factor-free medium (colonies growing in factor-free medium $\times$ 100/colonies growing in complete medium). All SV40-transformed clonal lines had efficiencies, in factor-free medium, of 20% to 60%, as did clonal lines transformed by sarcoma virus. The latter included a line transformed by the Moloney strain of MSV with associated leukaemia virus (G), two lines without associated leukaemia virus (one transformed by Moloney MSV (H) and one by Kirstein MSV (I)¹³) and one line transformed by RSV (J) without associated leukaemia virus. All the Balb 3T12 lines had high relative plating efficiencies in factor-free medium, and included a line (N) infected with murine leukaemia virus and three (K, L, M) with no demonstrable leukaemia virus¹⁴. In these conditions, the plating efficiency of Balb/c 3T3 was <0.1% (data not shown).

The virus-transformed and non-virus-transformed Balb/c 3T3 lines differed in their ability to grow in factor-free medium. Only three-eighths of the non-virus-transformants grew well; the remainder grew poorly, if at all. There was no correlation between the saturation densities of these lines (which ranged from $3.5\text{--}6.5 \times 10^5$ cells cm^{-2}) and their ability to grow in the absence of serum growth factor(s). Planting cells directly into factor-free medium, or shifting cells from complete to factor-free medium, gave similar relative plating efficiencies for all the lines except (P) which had an efficiency of only 1% after the cells were planted directly in factor-free medium although it increased to 125% after being planted first in complete medium. This line may require a serum factor lacking in factor-free medium to settle and flatten out¹⁵.

Our experiments confirm and extend the observation that all virus-transformed lines of Balb/c 3T3, as well as Balb/c 3T12, can grow in medium depleted of the serum growth factor(s). Furthermore, because most non-virus-transformed cells grow poorly, if at all, it is clear that loss of density dependent inhibition does not always result from a lowered requirement for these factors.

In virus transformations, there are two indications that loss of density dependent inhibition is not identical to decreased requirement for serum growth factor(s). First, the two properties are acquired at different times after SV40 infection: immediately after infection, Balb/c 3T3 cells become able to grow in factor-free medium¹² although several generations are necessary before the cells lose density dependent inhibition¹⁶. Second, there are SV40-transformed lines which have only one of the growth properties associated with virus-transformation, that is, the ability to grow in factor-free medium. Most of these lines may be the result of a secondary alteration as they were selected from a fully transformed line by FUDR¹⁷, but because there was no secondary selection involved in the development of two lines with these properties (ref. 13 and our unpublished observation) it is likely that the virus induced only the ability to grow in factor-free medium.

The simplest hypothesis consistent with all the data is that the two growth properties, that is loss of density dependent inhibition and loss of requirement for serum factor, are independent changes and that viruses usually induce both. Alternatively, there may be more than one way for a cell to lose density dependent inhibition. In virus-transformed lines and possibly in those non-virus-transformed lines that also grow in factor-free medium, the loss of requirement for serum factor may be necessary, but not sufficient, for the loss of density dependent inhibition. In other cases (that is most non-virus-transformed lines) a mechanism not dependent on the loss of

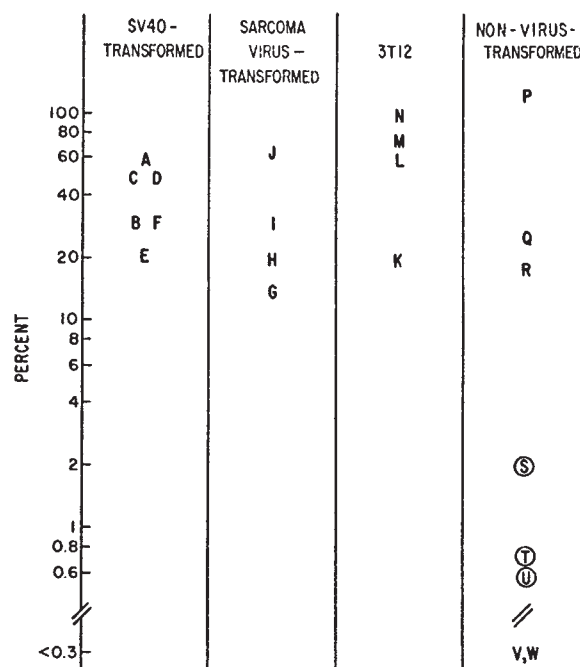


Fig. 1 Relative plating efficiency of transformed lines in medium lacking serum growth factors. Data are expressed as colonies growing in factor-free medium $\times$ 100/colonies growing in complete medium. Colonies were scored 2 weeks after planting. The circled letters indicate colonies that grew more slowly in factor-free medium and were scored, 3–4 weeks after planting. SV40-transformed lines: A, SV₁; B, SV₃; C, SV₄; D, SV₅; E, SV₆; F, SVT₂. Sarcoma virus transformed lines: G, MS24; H, 85-2; I, KA31CL₂₃₄; J, B77. Balb/c 3T12 lines: K, 3T12/1; L, 3T12/2; N, 3T12/3; M, 3T12/P13. Non-virus transformed lines: P, IIC12; Q, R-4; R, TA31; S, εA31; T, A31A1C11; U, 17C11; V, STA31; W, IC16.

serum factor requirement could also cause the loss of density dependent inhibition. Whichever hypothesis is correct, it is clear that these two growth properties are not identical.

We thank Dr S. Aaronson for many transformed lines, Miss K. Reynolds and Mrs K. Gottesman for technical assistance, and Dr G. Todaro for discussions and the hospitality of his laboratory. This work was supported by a contract from the National Cancer Institute.

HELENE S. SMITH *
CHARLES D. SCHER

National Cancer Institute,
Bethesda, Maryland, and
Mel-Labs Inc.,
Springfield, Virginia

Received November 10, 1970.

* Present address: Cell Culture Laboratory, School of Public Health, University of California, Berkeley, California.

¹ Todaro, G. J., and Green, H., *J. Cell. Biol.*, **17**, 299 (1963).

² Aaronson, S. A., and Todaro, G. J., *J. Cell. Physiol.*, **72**, 141 (1968).

³ Macpherson, J. A., and Montagnier, L., *Virology*, **23**, 291 (1964).

⁴ Black, P. H., *Virology*, **28**, 760 (1966).

⁵ Todaro, G. J., Matsuya, Y., Bloom, S., Robbins, A., and Green, H., in *Growth Regulating Substances for Animal Cells in Culture* (edit. by Defendi, V., and Stoker, M.), 87 (Wistar Institute Press, Philadelphia, 1967).

⁶ Holley, R. W., and Kiernan, J. A., *Proc. US Nat. Acad. Sci.*, **60**, 300 (1968).

⁷ Dulbecco, R., *Nature*, **227**, 802 (1970).

⁸ Clark, G. D., Stoker, M. G. P., Ludlow, A., and Thornton, M., *Nature*, **227**, 798 (1970).

⁹ Jainchill, J., and Todaro, G. J., *Expt. Cell Res.*, **59**, 137 (1970).

- ¹⁰ Temin, H. M., in *Growth Regulating Substances for Animal Cells in Culture* (edit. by Defendi, V., and Stoker, M.) (Wistar Institute Press, Philadelphia, 1967).
- ¹¹ Burk, R. R., *Nature*, **212**, 1261 (1966).
- ¹² Smith, H. S., Scher, C. D., and Todaro, G. J., *Virology*, **44**, 359 (1971).
- ¹³ Aaronson, S. A., and Rowe, W. P., *Virology*, **42**, 9 (1970).
- ¹⁴ Aaronson, S. A., Hartley, J. W., and Todaro, G. J., *Proc. US Nat. Acad. Sci.*, **64**, 87 (1969).
- ¹⁵ Fisher, H. W., Puck, T. T., and Sato, G., *Proc. US Nat. Acad. Sci.*, **44**, 4 (1958).
- ¹⁶ Todaro, G. J., and Green, H., *Proc. US Nat. Acad. Sci.*, **55**, 302 (1966).
- ¹⁷ Pollack, R. E., Green, H., and Todaro, G. J., *Proc. US Nat. Acad. Sci.*, **60**, 126 (1968).

Incidence of Mycoplasma Infection in Guinea-pigs

THE isolation of a new mycoplasma species, *Mycoplasma caviae*, was recorded recently¹. This species has been isolated from the nasopharynx and vagina of 10% of 232 guinea-pigs and is apparently non-pathogenic to these and other common laboratory animals. During this survey, no other known species of mycoplasma were isolated. (A strain of *M. caviae* G. 122 has been lodged in the National Collection of Type Cultures and has been given the reference number NC/TC 10126.)

Although we have failed to isolate other known species of mycoplasma from 232 guinea-pigs, it has been claimed that in Germany all guinea-pigs carry *M. pulmonis* in the vagina². It is interesting to speculate why the incidence of infection in Germany should be so different to that in the United Kingdom. Further information on the incidence of mycoplasma infection of guinea-pigs in different countries would be most interesting.

AURIOL HILL

MRC Laboratory Animals Centre,
Medical Research Council Laboratories,
Woodmansterne Road, Carshalton, Surrey

Received June 17, 1971.

¹ Hill, A., *J. Gen. Microbiol.*, **65**, 109 (1971).

² Juhr, von, N. C., and Obi, S., *Z. Versuchstierk.*, **12**, 383 (1970).

Transplacental Transmission of Endogenous Interferon in Pregnant Mice inoculated with Influenza or Newcastle Disease Viruses

THE possibility of intrauterine infection transmitted from affected mother to foetus has been established by both clinical^{7,11} and experimental^{3,6,9,10} investigations. Inoculation of pregnant animals with pathogenic viruses often brings about foetal infection resulting in impaired intrauterine development. When non-pathogenic strains are used, however, pregnancy may proceed normally and result in the birth of healthy offspring⁴. It has been demonstrated repeatedly that viruses with low pathogenicity for animals are effective producers of endogenous interferon. Preliminary administration of such interferon inducers has been shown to promote non-specific protection in animals against inoculation of lethal viruses^{5,8}.

In our investigation we used influenza A1/3711 virus and Newcastle disease virus (NDV) which were non-pathogenic for mice for interferon induction. These viruses are known to stimulate active production of endogenous interferon in mice, resulting in development of short term insusceptibility to subsequent inoculation with lethal influenza infection². The aim of our study was to test the possibility of transplacental transmission of endogenous interferon from mother to foetus

with resulting activation in the offspring of non-specific immunity to infection with various viruses.

Production of endogenous interferon was induced on days 17–21 of pregnancy by intranasal instillation of 0.2 ml. of allantoic fluid containing influenza A1/3711 virus, or by intravenous administration of 1.0 ml. of NDV. Both preparations contained 10⁶ ID₅₀/0.2 ml.

At different intervals after A1/3711 or NDV inoculation, sera and suspensions of washed lung, placenta and foetal tissues were tested for virus and interferon content. Serum and lungs of newborn mice were tested for the same. Interferon was titrated on mouse fibroblast tissue cultures in terms of suppression of cytopathogenic action of vesicular stomatitis virus. Influenza A1 virus or NDV were inactivated in these specimens by preliminary treatment in acid medium (pH 2.0).

Newborn mice from experimental or control (uninoculated) mothers were challenged on different postnatal days intranasally (0.06 ml.) with mouse-pathogenic allantoic influenza AO/PR8 virus of 10⁴ ID₅₀/0.2 ml. activity. The inoculated sucklings were observed for 1 month.

Inoculation of influenza A1/3711 virus or NDV 3–4 days before birth did not affect the course of pregnancy, and the offspring survived the observation period.

Intranasal inoculation of pregnant mice with influenza A1 virus resulted in subclinical infection, accompanied by significant accumulation of interferon in the lungs from the first day after inoculation. Maximal values of interferon activity were obtained on days 3–4, when the level in the lungs was two to four times higher than that in bloodstream, uterus, placenta or foetuses (Table 1).

Table 1 Interferon Levels in Serum and Organs of Mice inoculated with Influenza A1/3711 or Newcastle Disease Viruses on Days 17–18 of Pregnancy

Interferon induced with virus	Specimens tested	Time of interferon titration (h after inoculation)				
		6–8	24	48	72	96
Influenza A1/3711	Serum *	—	2	8	32	16
	Lungs †	—	4	8	64	64
	Uterus	—	2	4	8	4
	Placenta	—	2	8	8	8
	Foetus	—	2	4	8	8
Newcastle disease	Serum	512	128	32	16	4
	Uterus	64	16	4	—	—
	Placenta	64	32	4	2	—
	Foetus	64	24	4	2	—

* Activity of interferon in U/ml. of undiluted serum.

† Activity of interferon was tested in 50% suspension of washed organs and then was calculated on wet weight.

In contrast to influenza virus, NDV induced production of maximal interferon levels in circulating blood as early as 6–8 h after inoculation. At this time, high levels were found in uterus, placenta and foetuses (64 U/ml.).

The results of this investigation demonstrate the possibility of antenatal (intrauterine) transmission of non-specific resistance from mother to foetus. A positive correlation was found between intensity of interferon production in pregnant mice by term and the grade of resistance of their offsprings against lethal influenza infection. Mice born of experimental mothers were fully protected against fatal doses of influenza AO virus if the time of birth corresponded to peak interferon production in the mother. When birth occurred during a period of minimal interferon production in the mother, the extent to which the offspring were protected against influenza AO/PR8 virus decreased considerably (Table 2).

Influenza virus AO/PR8 was 100% fatal in the offspring of uninoculated (control) mice, at any postnatal age. But the offspring of females subjected to interferon induction during pregnancy and challenged on the first, third or fifth days after birth with the same fatal doses of influenza AO virus, survived the whole observation period. Complete protection of off-

Table 2 Non-specific Protection of Newborn Mice Against Fatal Influenza Infection Due to Antepartum Interferon Induction in Pregnant Mice with Influenza A1/3711 Virus and Newcastle Disease Virus

Interferon induced with virus	Day of pregnancy when interferon production induced	Sucklings challenged on postnatal day	Interferon level in sucklings	No. of sucklings	No. dying	Death rate (%)	Protection factor* (%)
Influenza A1/3711	17-18	1	1:8	12	0	0	100
		3	1:2	15	0	0	100
		5	—	17	0	0	100
		7	—	14	4	29.0	71
		10	—	10	4	40.0	60
	20-21	13	—	12	9	75.0	25
		16	—	9	9	100	0
		1	1:1	15	1	7.0	93
		3	—	13	4	30.0	70
		5	—	9	5	55.0	45
Newcastle disease	17-18	7	—	11	11	100	0
		1	1:1	17	3	17.0	83
		2	—	18	7	39.0	61
		4	—	16	10	63.0	37
	20-21	1	1:16	18	0	0	100
		3	1:2	17	0	0	100
		5	—	19	6	31.0	69
		7	—	12	5	42.0	58
		13	—	15	13	87.0	13

* Compared with groups of control sucklings in which influenza AO virus caused 100% death, at any age after birth.

spring was demonstrated in animals born at the time of peak interferon production induced in mothers with A1/3711 virus or NDV.

When older sucklings (7-13 days after birth) were challenged, their protection against influenza virus AO/PR8 was found to have diminished, but still persisted at the 50-70% level, while death was delayed (for 3-4 days), compared with control sucklings.

Protection of newborn mice may be effected by relatively low concentrations of interferon, which cannot be detected by current methods of titration. This is confirmed by the results of titration of influenza AO/PR8 virus on the 3 day old offspring of mothers in whom interferon had been induced with NDV 1 day before term. Animals which received maternal interferon before birth proved to be fully resistant to AO virus. Interferon circulating in their bloodstream (1:2 titre) neutralized 10^5 infective doses of the challenging virus (Table 3). This is supported by tissue culture experiments¹.

Table 3 Titration of Influenza AO/PR8 Virus on 3 Day Old Offspring of Mice exposed to Interferon Induction with Newcastle Disease Virus inoculated on Days 18-19 of Pregnancy

Groups of sucklings	Challenged with dilutions of influenza AO/PR8 virus						
	10^{-1}	10^{-2}	10^{-3}	10^{-4}	10^{-5}	10^{-6}	10^{-7}
Born of mothers exposed to interferon induction	18	17	14	10	8	6	
Died when resistance challenged	7	2	0	0	0	0	
Death rate (%)	39.0	12.0	0	0	0	0	
Born of control mothers	4	8	7	9	14	13	6
Died	4	8	7	9	10	4	0
Death rate (%)	100	100	100	100	71.0	31.0	0

These studies confirm the possibility of protecting mice antenatally against postnatal fatal influenza infection. Here, the leading part belongs to endogenous interferon, which penetrates the placenta and creates in the foetus a state of resistance against virus infection. The significance of maternal interferon in protection of newborn mice is supported by

experiments in which normal newborn sucklings were inoculated with influenza A1/3711 virus at different postnatal days. No interferon could be detected in the lungs of mice inoculated within the fifth to seventh postnatal days. With age, however, the production of interferon increased.

B. M. KORSANTIYA

AL. A. SMORODINTSEV

All-Union Research Institute of Influenza,
Leningrad, and
Research Institute of Hygiene,
Tbilisi

Received August 4; revised November 23, 1970.

- Korsantiya, B., Gvozdiolova, D., and Smorodintsev, Al., *Tsitologia*, **9**, 1304 (1967).
- Smorodintsev, Al., Gvozdiolova, D., and Aksenov, O., in *Interferon*, **93** (1970).
- Soloviev, V., Khesin, Y., and Gutman, N., *Vopr. Virus.*, **1**, 60 (1970).
- Ferm, V., and Low, R., *J. Pathol. Bact.*, **89**, 295 (1965).
- Isaacs, A., and Hitchcock, G., *Lancet*, **ii**, 7141, 69 (1960).
- Middelkamp, I., Reed, C., and Patrizi, G., *Proc. Soc. Exp. Biol. Med.*, **125**, 757 (1967).
- Mitchell, I., and McCall, F., *Amer. J. Dis. Child.*, **106**, 207 (1963).
- Rytel, M., *J. Gen. Virol.*, **3**, 429 (1969).
- Soike, K., *J. Inf. Dis.*, **117**, 203 (1967).
- Takeyama, T., *Tohoku J. Exp. Med.*, **89**, 321 (1965).
- Witzleben, C., and Driskoll, S., *Pediatrics*, **36**, 192 (1965).

Genetic Recombination in Malaria Parasites

THE complexity of the life cycle of malaria parasites and the lack of suitable strain characters which could be used as genetic markers have made genetic studies of these organisms difficult. We have now available, however, a number of strains of *Plasmodium berghei* isolated from wild rodents and mosquitoes in Africa, which can be differentiated from one another by starch-gel electrophoresis of certain enzymes¹. We have also derived parasite lines resistant to the drug pyrimethamine from some of these strains, and such resistant lines remain stable even in the absence of the drug. By making crosses between lines which differ in both enzyme type and drug sensitivity, we have been able to obtain parasites exhibiting recombinant characters.

The parasite lines selected for use are described here as lines A and C. Line A was derived from strain 17X of *P. b. yoelii* and is pyrimethamine resistant. The resistance was produced in a single step² by treating mice infected with strain 17X with pyrimethamine at doses of 50 mg/kg daily for 4 days. Line A, like strain 17X, contains the electrophoretic form of the enzyme glucose phosphate isomerase denoted GPI-1¹. Line C was derived from strain 33X of *P. b. yoelii*, and is pyrimethamine-sensitive. In the 4 day suppressive test³, it is more than fifty times as sensitive to pyrimethamine as line A. Line C contains the enzyme form GPI-2¹.

The sequence in which this work was conducted is presented in Fig. 1. Equal amounts of blood (0.3 ml.) were taken from two tree rats (*Grammomys surdaster*), one of which was infected with line A and the other with line C. The blood from each animal was mixed and injected intravenously into an uninfected tree rat. This produced an immediate patent parasitaemia in the recipient (113 A+C in Fig. 1). Mosquitoes (*Anopheles stephensi*) were fed immediately on this animal in the hope that gametes of each strain would mix. The resulting sporozoites were used to infect further tree rats from which ten C57 black mice (127 A+C in Fig. 1) were subsequently infected. Five of these mice were treated with subcutaneous doses of pyrimethamine⁴ at 15 mg/kg daily for 4 days. All ten mice became infected and examination of the parasites on starch gels (Fig. 2) revealed the presence of both GPI-1 and GPI-2 in all animals.

To confirm that the GPI-2 parasites in the treated mice were drug-resistant, infected blood from these mice was diluted in serum Ringer⁵ into aliquots containing an average of one parasitized cell. The aliquots were inoculated into individual mice, from which blood infections were established. Two GPI-1 and two GPI-2 lines were derived in this way, each of which was found to grow equally well when subjected to pyrimethamine treatment.

As controls the parent lines A and C were passed through mosquitoes, tree rats and mice in the same way as the mixture. Line A parasites survived drug treatment, and line C parasites were eradicated. The work has been repeated several times with similar results; line C has been exposed to pyrimethamine at doses of 15 mg/kg in fifty mice, none of which has remained infected. We think it very unlikely, therefore, that mutation could account for the appearance of resistant GPI-2 parasites in the mixed infections.

Two further controls were set up to determine whether the recombinant parasites obtained were due to the phenomenon described by Yoeli *et al.*⁴ as "synpholia". In synpholia, it is suggested that pyrimethamine resistance can be transferred from one strain to another when they grow up together in blood cells of the same host. In the first control, tree rat 113A+C (inoculated with equal numbers of blood parasites of each line) was kept alive for 7 days after mosquitoes had fed on it. Blood parasites from this animal were then used to infect ten mice, five of which were treated with pyrimethamine. In these mice, only GPI-1 parasites survived, but in the untreated mice both GPI-1 and GPI-2 parasites were present. In the second control, sporozoites of each parent line were pooled and inoculated into tree rats. After five days, blood parasites from these animals were used to infect ten mice, five of which were given pyrimethamine. In untreated animals, both GPI-1 and GPI-2 parasites were detected, while the animals given pyrimethamine contained only GPI-1 parasites after treatment.

We have been unable, therefore, to produce parasites exhibiting recombinant characters by simply mixing blood parasites or sporozoites of the parent lines. This does not disprove the phenomenon of synpholia, which may occur as a rare event detectable only when double selection pressure is applied⁴, but suggests that it cannot account for our results.

We consider that these results are important in two respects. First, they show that a conventional genetic analysis of malaria parasites is possible. This should enable us to obtain much

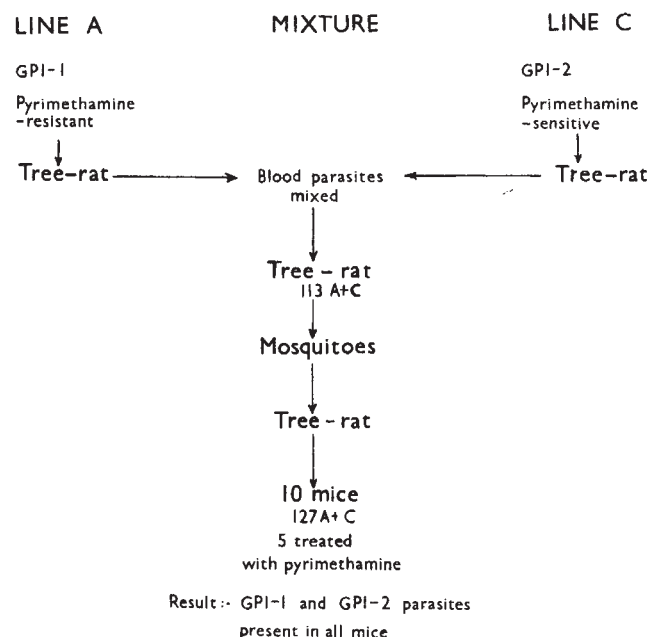


Fig. 1 Procedure adopted in producing recombinant parasites.

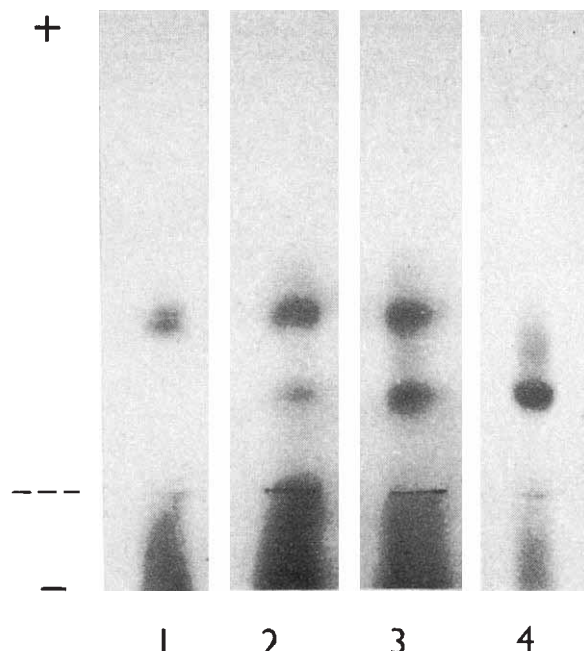


Fig. 2 Starch gel zymograms of glucose isomerase (GPI) in line A, line C, and mixtures of lines A and C. 1, Line A (GPI-1); 2, mixture following pyrimethamine treatment of mice 127A+C (showing GPI-1 and GPI-2); 3, mixture in untreated mice 127A+C (showing GPI-1 and GPI-2); 4, line C (GPI-2).

more precise information than has been available hitherto on the biological basis of such important characters as drug resistance and virulence. Second, they indicate that genetic recombination is continually taking place in natural populations of malaria parasites, which enables the rapid evolution of new strains and their spread in populations of animals and man. We propose to exploit the technique outlined here to investigate the nature of other types of drug resistance as well as enzyme polymorphism and virulence.

We thank Mr A. Sanderson for technical assistance. This work is supported by a grant from the Medical Research Council to Professor G. H. Beale.

D. WALLIKER
R. CARTER
S. MORGAN

Protozoan Genetics Unit,
Institute of Animal Genetics,
University of Edinburgh,
Edinburgh EH9 3JN

Received April 21; revised May 10, 1971.

- ¹ Carter, R., *Trans. Roy. Soc. Trop. Med. Hyg.*, **64**, 401 (1970).
- ² Diggins, S. M., Gutteridge, W. E., and Trigg, P. I., *Nature*, **228**, 579 (1970).
- ³ Peters, W., *Exp. Parasitol.*, **17**, 80 (1965).
- ⁴ Yoeli, M., Upmanis, R. S., and Most, H., *Parasitology*, **59**, 429 (1969).
- ⁵ Warhurst, D. C., and Folwell, R. O., *Ann. Trop. Med. Parasitol.*, **62**, 349 (1968).

Frequency Analysis of the Thirst Control System

DRINKING is essential for the homeostasis of body fluids, and a theoretical structure which makes the principles and details of homeostasis explicit is provided by control theory. A control model of thirst has been described by Oatley^{1,2} and simulated on a digital computer³.

Responses to sinusoidally varying stimuli can give quantitative information about the structure of biological control systems^{4,5}, and we present here an analysis of drinking by rats in response to sinusoidal salt injections and compare it with the simulated drinking response of the model³. We show how frequency analysis applied to a system which has non-linear components (for example, a threshold), can indicate the relative importance of linear and non-linear components.

Sinusoidal infusions of sodium chloride were given at frequencies of 1, 2, 4 and 8 cycles per hour (c.p.h.) to sixteen albino rats chronically implanted with jugular cannulae made of silicone rubber tubing. The mean body weight of the rats was 387 g, and this value was also used for the simulation. The injection waveform was controlled by pulsing an infusion pump at intervals varying sinusoidally with time. The flow rate of hypertonic salt solution into the rat produced in this way approximated the equation:

$$A + A \cos \omega t \quad (1)$$

where A is the mean rate, 0.0544 mequiv. of Na/min. The infusion varied between zero and $2A$ mequiv./min. The concentration of the salt was 3 M, and injections were continued until a sufficient number of cycles (a minimum of 4 at 1 c.p.h. and a maximum of 24 at 8 c.p.h.) had been accomplished. All rats drank water in response to at least one infusion frequency (each rat had one frequency per day) but clotting of cannulae sometimes occurred so that some rats had to be discarded. They were also relieved of further duty if signs of discomfort appeared during injection. Although we collected between eight and ten readings at each frequency, only three of the rats ran satisfactorily through all four.

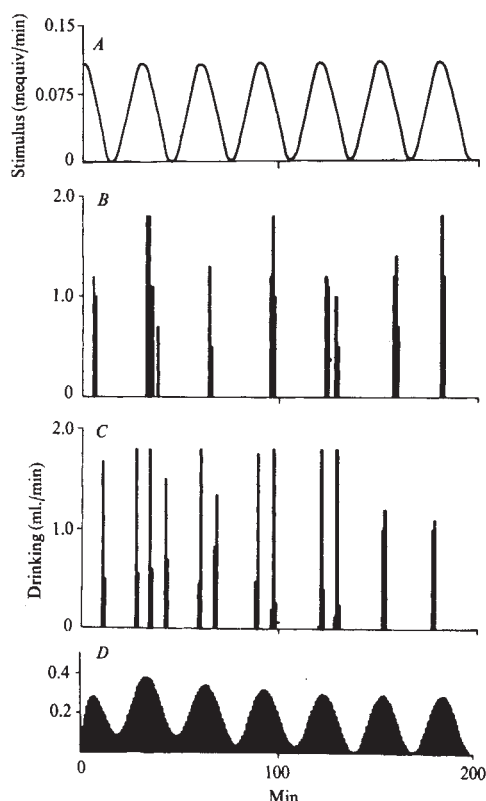


Fig. 1 Sinusoidal input infusion at 2 c.p.h., and histograms of drinking responses to it: (A) input infusion defined by equation (1); (B) typical experimental result showing one rat's drinking response; (C) computer simulation response run with threshold; (D) computer simulation response run without threshold. The histograms (B, C and D) represent drinking rate, with the height of each vertical bar showing the volume of water drunk in each 1 min period of the 200 min test. Note that the vertical scale for histogram (D) is exactly twice that of histograms (B and C).

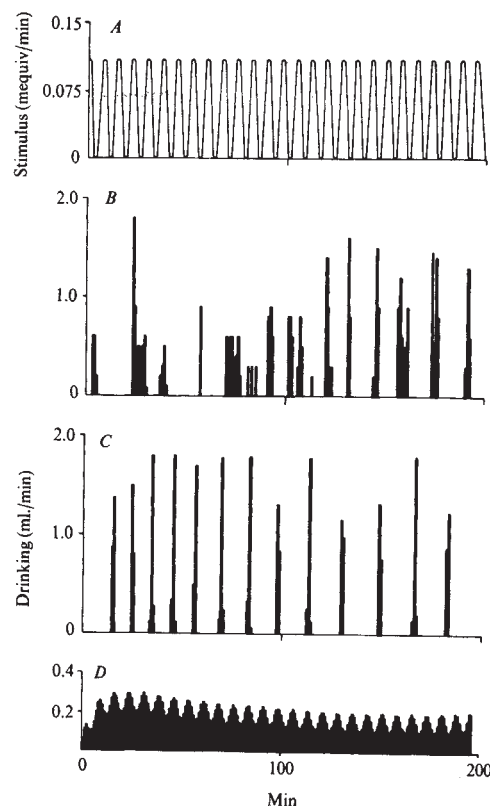


Fig. 2 Sinusoidal input infusion at 8 c.p.h. and histograms of drinking responses to it. Except for the higher frequency the description is as for Fig. 1.

Fig. 1b shows a typical response to a 2 c.p.h. stimulus, and Fig. 1c shows the computer simulation of this experiment. At 1 and 2 c.p.h., responses consistently showed the same dominant frequency as the input stimulus. In the 4 and 8 c.p.h. results, the pseudo-linear following of the input frequency that occurred at the lower frequencies failed to occur. Instead of transmitting the 4 and 8 c.p.h. signals, animals and simulation responded by an oscillation of drinking at a lower frequency (Fig. 2).

The principal non-linear component in the system is a threshold, which the deficit of body water must reach for drinking to be initiated. Toates and Oatley³ reviewed experiments in which the value of the threshold has been measured, and took 0.7 ml./100 g body weight as a typical value, which also fitted experiments reported in that article, as well as the data reported here. When the threshold was removed from the simulation, the computer followed input frequencies throughout the range tested, that is, 0.16 to 30 c.p.h. This response, without the threshold, was totally different from that of rats or of the complete simulation (Figs. 1d and 2d).

Frequency response methods are most useful for linear systems, but an output from non-linear systems can be approximated by a sinusoid at the input frequency and of an appropriate amplitude and phase. A computer program was written to perform the fitting procedure. It searched each combination of amplitude and phase to find the best sinusoidal fit to the drinking data, using as a criterion the minimum value of the square of the error at each point summed over the time observed. Functions were fitted after discarding the first 30 min of the drinking response, to exclude the major part of transient effects.

The open circles in Fig. 3 show the gain and phase of the sinusoids that best fitted the response of the model without the threshold, measured at several frequencies. This response approached a maximum phase shift of -90° , characteristic of a

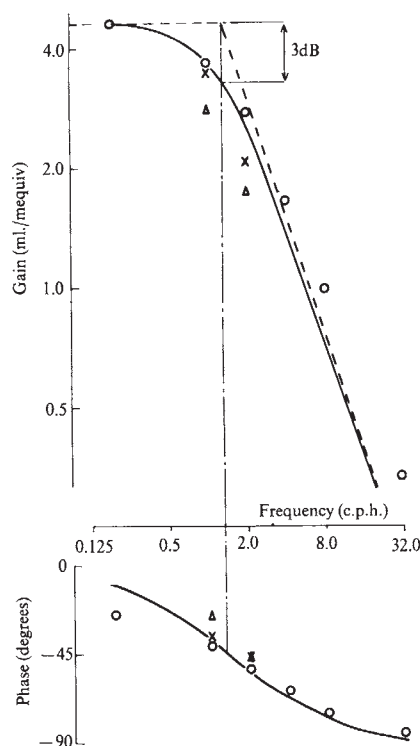


Fig. 3 Gain (expressed as drinking rate in ml./min, divided by input infusion rate in mequiv. of Na/min) and phase plots of frequency responses. The solid lines represent the function $K/(1 + \tau s)$, with $\tau = 0.12$ h, the lines - - are the low and high frequency asymptotes to this function, and the line — indicates their intersection at a frequency equal to $1/2\pi\tau$. Best fitting sinusoidal frequencies for experimental data and computer runs are shown by: (Δ) mean experimental results; ($\times$) computer simulation, with threshold; ($\circ$) computer simulation without threshold.

first order system described by the transfer function

$$H(s) = \frac{K}{1 + \tau s} \quad (2)$$

where K is the gain constant, τ the time constant, and s the Laplace operator.

McFarland and Budgell⁶ found a transfer function for key pecking by thirsty birds in response to modulations of ambient temperature which was of the same kind as this drinking response to salt injections, though it had a slightly smaller time constant.

The phase lag of a first order system is given by: $\arctan \omega\tau$, where ω is the radian frequency per unit time. The mean value of τ calculated from the phase results of the simulation without the threshold was 0.12 h (7.2 min) and with this value, the gain and phase given by equation (2) are shown as solid lines in Fig. 3.

Though the simulation contains non-linearities other than the threshold, Fig. 3 shows the gain of the simulation without threshold to be well fitted by this first order characteristic; and the phase also, except at the lowest frequencies. The best fitting sinusoidal responses for the experimental results and for the simulation with threshold at 1 and 2 c.p.h. are also plotted on Fig. 3 and both gain and phase approach that of the first order approximation. Since frequency following was abolished at 4 and 8 c.p.h. no points could be plotted for these frequencies.

An overall transfer function such as equation (2), can give some idea of the basic structure of a biological system. In this case the first order function arises because rates of flow into and out of body fluid compartments (hypertonic saline causes

flow of water out of the cellular compartment) are integrated, and drinking acts as a feedback signal, restoring deficits. An integrator with feedback around it constitutes just such a first order system as described by equation (2), but frequency analysis applied to the real system and to the model³ indicates that characterization of the system as first order with $\tau = 0.12$ h is only a superficial description of the system. It gives no clue as to how physiological processes make up the total system. In comparison with the three components (summing junction, integrator and constant coefficient) required to represent the first order transfer function (2), the block diagram of our simulation³ which contains a minimal representation of the physiological events that control thirst and body water, has eighty-seven such elements. Clearly there are limits to the adequacy with which transfer functions derived from overall linear frequency analysis can represent what is going on in biological control systems.

In this analysis, however, frequency methods have first confirmed the adequacy of the model³ (built on a physiological understanding of the component processes and with no arbitrary components or *ad hoc* alteration of parameters) to represent the real system and to generate an overall drinking response comparable with that of a real animal; and, second, these methods establish the relative importance of linear and non-linear features of the system. The time constant (0.12 h) of the system estimated from this small signal analysis differs from the estimate of 0.5 h, in response to a single large transient injection of 2.73 mequiv. of sodium³. Thus even the pseudo-linear behaviour at lower frequencies provides evidence for non-linearity, which for large signals is due to non-linear inhibition of drinking by large volumes of water in the stomach.

The claim by Corbit⁶ that there is no threshold for drinking in response to hypertonic NaCl seems to be refuted, for in these experiments the threshold dominated the form of the response. Apart from making drinking intermittent at all frequencies (see Figs. 1 and 2, b and c) a threshold with hysteresis³ was able to account for the fact that drinking of neither the model nor the rat was able to follow the input at higher frequencies. At 4 and 8 c.p.h. the integral of the rate of salt injected in any one cycle was not sufficient to exceed the threshold. Instead drinking in response to these frequencies was similar to that for a steady infusion at the same mean rate; it exhibited a relaxation oscillation as a function of the mean infusion rate and the threshold value. For the simulation with the threshold the frequency of the relaxation oscillation was approximately 3.5 c.p.h. (Fig. 2). Thus, although with infusions of 1 and 2 c.p.h. no rat ever missed drinking in response to any cycle of the input, at 4 and 8 c.p.h., cycles were missed. It is not easy to say exactly at what frequency the drinking response oscillates for these inputs (Fig. 2b); it was less than the driving frequency, and of the order of 3.5 c.p.h. as shown by the model.

The role of the threshold for drinking may be as part of a mechanism which allows the animal to distribute its time between drinking and other systems that can control behaviour.

We thank D. A. Tonge for help in implanting cannulae, and the MRC for making this assistance possible.

KEITH OATLEY
F. M. TOATES

Laboratory of Experimental Psychology,
University of Sussex,
Brighton

Received January 4; revised April 5, 1971.

¹ Oatley, K., *Med. Biol. Eng.*, **5**, 225 (1967).

² Oatley, K., *Nature*, **225**, 797 (1970).

³ Toates, F. M., and Oatley, K., *Med. Biol. Eng.*, **8**, 71 (1970).

⁴ Milsum, J. H., *Biological Control Systems Analysis* (McGraw-Hill, New York, 1966).

⁵ Stark, L., *Neurological Control Systems* (Plenum Press, New York, 1968).

⁶ McFarland, D. J., and Budgell, P. W., *Nature*, **226**, 966 (1970).

⁷ Corbit, J. D., *J. Comp. Physiol. Psychol.*, **67**, 3 (1969).

One, Two or Three Connecting Links between Triassic and Jurassic Ammonoids?

It has long been recognized that the Jurassic and Cretaceous ammonoids are very different from those of the Triassic and it is generally concluded that the whole order Ammonoidea nearly became extinct at the Triassic-Jurassic boundary. More than a century ago Suess¹ recognized that one group, the phylloceratids, was common to both systems. Most authors²⁻⁵ have accepted this view and have further concluded that the phylloceratids provide the only link between the faunas of the Triassic and the Jurassic. In taxonomic terms this is expressed by Arkell *et al.*⁵ as follows: Jurassic and Cretaceous ammonoids comprise suborders Phylloceratina, Lytoceratina and Ammonitina. Of these only Phylloceratina extend back into the Triassic. In the Lower Triassic, Phylloceratina merge with Ceratitina, the dominant Triassic group, which became extinct at the end of the Triassic. It was the opinion of Arkell *et al.* that both Lytoceratina and Ammonitina were derived from Phylloceratina.

Wiedmann⁶ has now brought forward a very different interpretation, indicating that both Lytoceratina and Ammonitina lived in Triassic times and that the faunal break is much less profound than supposed by all previous workers, with three groups (Phylloceratina, Ammonitina and Lytoceratina) crossing the boundary. Schindewolf, Shv'yev and Teichert, as mentioned below, also agree that the Lytoceratina extend back to the Triassic. Wiedmann's recognition of Ammonitina in the Triassic is wholly novel.

I suggest that there is still no satisfactory evidence that Lytoceratina and Ammonitina are represented in the Triassic faunas and that Wiedmann's conclusions are not justified.

The recognition of Lytoceratina in the Triassic is based on one specimen, named *Trachyphylites costatus* by Arthaber⁷. To Arthaber, *Trachyphylites* was a subgenus of *Monophylites* (Phylloceratina). He noted resemblances between *Trachyphylites* and Lower Jurassic Lytoceratina but attributed them to convergence. Later workers^{2,8-12} have considered these resemblances to be of phylogenetic significance. There is now general agreement, which I do not dispute, that *Trachyphylites* is a representative of Lytoceratina, but is it a Triassic ammonoid? N. J. Silberling has drawn my attention to good reasons for suggesting that it may be Jurassic, not Triassic. The unique specimen of *Trachyphylites costatus* was collected by a Dutch expedition from a limestone block in Oë Bihati, about 2 km east of Baun in Indonesian Timor. Collections were made from numerous blocks in this river. Most were Triassic ammonoids but some of Jurassic age were also obtained. Individual blocks were designated by numbers and Greek letters. Their exact location in the river bed is shown on a map published by Burck¹³. Arthaber⁷ gives Bihati lower case theta (θ) as the locality for *T. costatus* in his text, but as lower case delta (δ) on the plate description. With the exception of *Rhacophylites fallax* Arthaber, which has the same ambiguous locality data, no other ammonoids have been recorded from block δ . Arthaber⁷ wrote that Diener noted the occurrence of both Triassic and Jurassic ammonoids from Bihati δ . But in Diener's report¹⁴ a mixing of Triassic and Jurassic ammonoids was recorded only from Bihati upper case theta (Θ). Diener makes no reference to Bihati δ . Burck's map shows both block δ and block Θ , but no θ . This suggests that both Θ and θ refer to the same block. There seems to be at least an even chance, therefore, that *Trachyphylites costatus* came from a block ($\Theta = \theta$) which contained both Triassic and Jurassic ammonoids. The exact age of *Trachyphylites* can only be considered uncertain. Nothing like *Trachyphylites* has been found in Triassic rocks elsewhere, but comparable ammonites occur in the Lower Jurassic according to Spath² and Basse⁸. Extending the range of Lytoceratina into the Triassic on this occurrence alone seems

unwarranted. *Trachyphylites* is probably what it looks like, a Jurassic ammonite.

The alleged extension of Ammonitina back into the Triassic must now be considered. Wiedmann⁶ describes a new genus, *Phyllytoceras*, based on Upper Triassic specimens from Iran and Austria. *Phyllytoceras* is classified as a member of a new family (Phyllytocerataceae) of Psilocerataceae (Ammonitina) by Wiedmann. He regards *Phyllytoceras* as the ancestor of *Psiloceras*, of the basal Jurassic Hettangian Stage; and possibly also the ancestor of Lytoceratina. *Phyllytoceras intermedium* Wiedmann, the only species known, is a smooth serpenticone. The suture line is ammonitic, with two lateral lobes, a dependent suspensive lobe, a non-lituid internal lobe, and a deep incision on the outer side of the external saddle. I submit that all these characters are found in the Gymnitidae, a family of Triassic Ceratitina. Many Gymnitidae are smooth serpenticones. They have ammonitic suture lines, with two lateral lobes, a dependent suspensive lobe and commonly a deep incision on the outer side of the external saddle¹². Gymnitidae attain a large size and have a more deeply incised suture line than *Phyllytoceras*. *Phyllytoceras* is known only from small specimens, however, the largest being 4.5 mm in diameter, so the differences in degree of incision are probably not significant. The internal lobe of *Japonites* (generally considered a gymnitid) is known to be non-lituid¹², as in *Phyllytoceras*. Non-lituid internal lobes have also been illustrated for *Tropigymnites planorbis* (Hauer)¹⁵ and *Arctogymnites sonini* Popov¹⁶. These two, if not Gymnitidae, are not far removed from members of the family. Wiedmann seems to be unaware that Gymnitidae have non-lituid internal lobes because he indicates that a lituid internal lobe is diagnostic of Ceratitina¹⁷. Also, he makes no comparison between the suture lines of *Phyllytoceras* and Gymnitidae. The non-lituid internal lobe of *Phyllytoceras* evidently influenced Wiedmann in his decision to regard it as a representative of Ammonitina, but clearly, this character is not decisive. Wiedmann⁶ has exposed the primary suture line of *Phyllytoceras*, showing it to have four lobes. The primary suture line of *Gymnites* and allied genera has not yet been described so the significance of this character of *Phyllytoceras* cannot be assessed at present. Most Triassic Ceratitina, however, have four-lobed primary suture lines¹⁷. Psilocerataceae, and most, if not all, other Ammonitina have five-lobed primary suture lines¹⁷. The four-lobed primary suture line of *Phyllytoceras*, therefore, in no way supports its assignment to Ammonitina. There seems to be no doubt that *Phyllytoceras* is a member of Gymnitidae, possibly an immature representative of *Gymnites* itself. Suture lines of Psilocerataceae^{5,6,18} do not closely resemble those of *Phyllytoceras* and *Gymnites*. All have dependent suspensive lobes but the Psilocerataceae lack the deep incision in the external saddle that gives character to the suture lines of *Gymnites* and *Phyllytoceras*.

I conclude that there is no good evidence that Lytoceratina and Ammonitina are represented in the Triassic ammonoid fauna. The Triassic-Jurassic faunal break is as profound as believed by Arkell *et al.*⁵ and there is still only one group, the phylloceratids, known to straddle the boundary.

E. T. TOZER

Geological Survey of Canada,
Department of Energy, Mines and Resources,
601 Booth Street,
Ottawa, Ontario

Received March 22, 1971.

¹ Suess, E., *Sitzungber. Akad. Wiss. Math.-Naturwiss. Kl.*, **52** (I-II), 1, 71 (1865).

² Spath, L. F., *Cat. Fossil Cephalopoda Brit. Mus. (NH)*, Part IV (1934).

³ Arkell, W. J., *J. Paleontol.*, **24**, 354 (1950).

⁴ Donovan, D. T., *Biol. Rev. Cambridge Phil. Soc.*, **39**, 259 (1964).

⁵ Arkell, W. J., *et al.*, *Treatise on Invertebrate Paleontology*, Part L (Geol. Soc. Amer., and Univ. Kansas Press, 1957).

⁶ Wiedmann, J., *Eclogae Geol. Helv.*, **63**, 923 (1970).

- ⁷ Arthaber, G. v., *Jb. Mijnw. Ned. Oost.-Ind.*, **55**, 1 (1927).
⁸ Basse, E., in *Traité de Paléontologie* (edit. by Piveteau, J.), **2**, 461 (Masson, Paris, 1952).
⁹ Schindewolf, O. H., *Akad. Wiss. Lit. Mainz, Abh. Math.-Naturwiss. Kl.*, 1960, 635 (1961).
¹⁰ Teichert, C., *Univ. Kansas Dept. Geol. Spec. Publ.* **2**, 162 (1967).
¹¹ Wiedmann, J., *Neues Jb. Geol. Paläontol. Abh.*, **125**, 49 (1966).
¹² Shevyrev, A. A., *Tr. Paleont. Inst. Akad. Nauk. SSSR*, **119** (1968).
¹³ Burck, H. D. M., *Jb. Mijnw. Ned. Oost.-Ind.*, **49**, 1 (1923).
¹⁴ Diener, C., *Jaarb. Mijnw. Ned. Oost.-Ind.*, **49**, 73 (1923).
¹⁵ Hauer, F. v., *Denkschr. Akad. Wiss. Wien*, **63**, 237 (1896).
¹⁶ Popov, Yu. N., *Tr. Nauch.-Issled. Inst. Geol. Arktiki*, **79** (1961).
¹⁷ Kullmann, J., and Wiedmann, J., *Univ. Kansas Paleontol. Contr.*, **47** (1970).
¹⁸ Frebold, H., *Geol. Survey Canada Bull.*, **158** (1967).

Cranium of *Plesiadapis*

THE reconstruction by Szalay of the only known skull (CR 125, Muséum National d'Histoire Naturelle, Paris) of the Palaeocene primate *Plesiadapis* was presented¹ as differing from previous reconstructions²⁻⁴ in the occlusal relationship of the enlarged procumbent incisors and in the relationship of the bones of the snout.

Szalay's principal contribution was his supposedly new location posteriorly of the point of occlusion of the lower incisors with the uppers. The incisor relationship illustrated by Szalay is not new, however; it is precisely that illustrated in the original reconstruction of this skull by Simons² (Fig. 1). Szalay refers to this 1960 reconstruction but does not discuss it, preferring to address his comments to a derived illustration which accompanied a popular article written later by Simons³.

Reconstruction of the snout of this animal by Russell⁴ was prefaced by the remark "L'écrasement subi a rendu difficile la détermination de la limite postérieure et dorsale des pré-maxillaires". This remains true. Russell's discussion, together with Szalay's Fig. 2, support the original interpretation of bone relationships of the snout by Russell^{4,5}, not that newly

presented by Szalay. A premaxillary-frontal contact is present in living mammals with procumbent *Plesiadapis*-like incisors (compare the marsupial *Dactylopsila*, the primate *Daubentonia*, rodents and lagomorphs) and is probably related to the function of such incisors. Until better preserved material is discovered, Russell's original interpretation that the premaxilla makes contact with the frontal in *Plesiadapis* remains the most reasonable alternative.

Szalay also criticizes the statement by Simons and Russell⁶ that "only in Cheirogaleinae, among living and fossil Lemuriformes, is the os planum present" and cites Forsyth Major⁷ as evidence for disagreeing with them. In fact, what Forsyth Major said was: "Amongst the Malagasy Lemurs a fairly large os planum is present in all the species of *Microcebus*. In the other genera the planum becomes fused with the palatal at a very early date". Thus Forsyth Major's evidence agrees with Simons and Russell's statement, not with Szalay's. A distinct os planum is present in mature skulls of Lemuriformes only in the Cheirogaleinae (including *Microcebus*) (see ref. 8 for a more recent discussion).

Szalay objects to the use of the presence of an os planum in the orbital wall as a diagnostic feature of the order Primates. As Le Gros Clark outlined⁹, and Martin restated¹⁰, any definition of primates must be based on a suite of characters, a "total morphological pattern" or a "total functional pattern", not all of which will be present in all forms included in the order. Absence of an os planum in certain early Tertiary primates and some living lemurs does not preclude using the presence of an os planum as one of a suite of characters defining the order primates; an os planum is present in most primates.

In short, Szalay's recent article contributes no addition to knowledge of the cranial or dental anatomy of *Plesiadapis*.

PHILIP D. GINGERICH

Department of Geology and Geophysics, and
 Peabody Museum of Natural History,
 Yale University,
 New Haven, Connecticut 06520

Received April 29, 1971.

- ¹ Szalay, F. S., *Nature*, **230**, 324 (1971).
² Simons, E. L., *Amer. Sci.*, **48**, 179 (1960).
³ Simons, E. L., *Sci. Amer.*, **211**, 51 (1964).
⁴ Russell, D. E., *Mém. Mus. Nat. Hist. Nat.*, **C**, **13**, 1 (1964).
⁵ Russell, D. E., *Bull. Soc. Géol. Fr.*, ser. 7, **1**, 312 (1959).
⁶ Simons, E. L., and Russell, D. E., *Breviora*, **127**, 1 (1960).
⁷ Forsyth Major, C. I., *Proc. Zool. Soc. Lond.*, **1**, 129 (1901).
⁸ Charles-Dominique, P., and Martin, R. D., *Nature*, **227**, 257 (1970).
⁹ Le Gros Clark, W. E., *The Antecedents of Man* (Edinburgh University Press, 1962).
¹⁰ Martin, R. D., *Man*, **3**, 377 (1968).

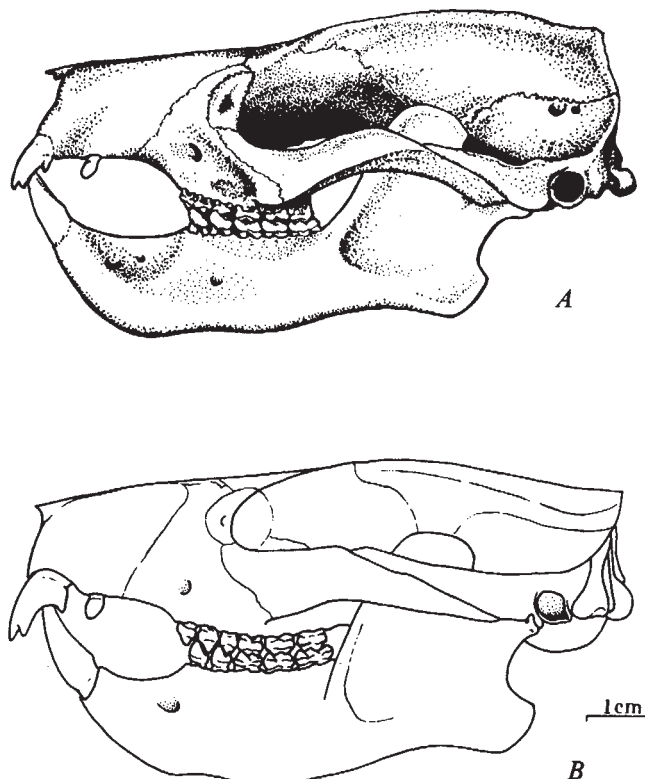


Fig. 1 Reconstructions of lateral view of skull of *Plesiadapis tricuspidens*. A, Original reconstruction by Simons (ref. 2); B, reconstruction by Szalay (ref. 1).

Ethmoid Component in the Orbit of Primates

SZALAY¹ has attributed to Forsyth Major² the statement that the ethmoid bone appears in the medial orbital wall of many Madagascar prosimians. But in fact, an orbital exposure (os planum) of the ethmoid is known only in *Cheirogaleus* and *Microcebus* among Lemuriformes. As Jones³ and Kollman⁴ have demonstrated, the element which Forsyth Major mistook for an os planum is the pre-nasopalatine part of the palatine bone.

The ethmoid of mammals is a cartilage-replacement bone which forms in the cartilaginous walls of the embryonic nasal chamber. In most non-primates, the ethmoid is covered by membrane bones laid down by the periorbita that lines the eye socket. If the orbits are very large or very close together, the periorbita is pressed against the nasal capsule in the

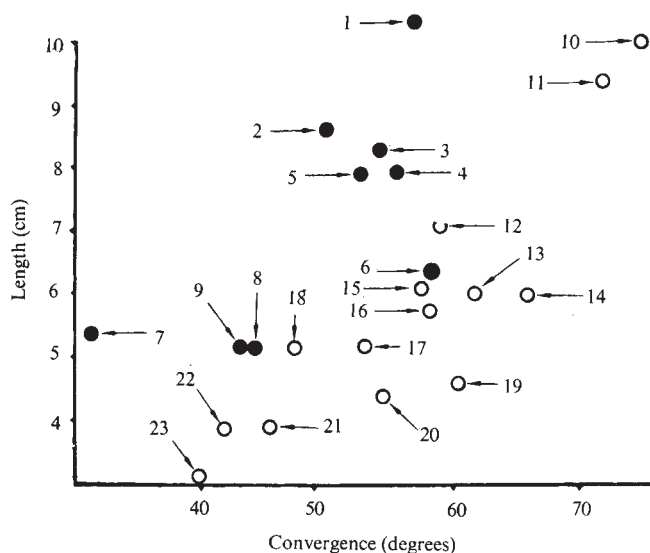


Fig. 1 Sample means of orbital convergence and prosthionion length in anthropoid and prosimian primates. "Convergence" is defined as the dihedral angle between the mid-sagittal plane and the plane of the medial orbital margin. Open circles represent species with an os planum in the medial orbital wall. Numerical designations (and sample sizes) of sampled species: 1, *Indri indri* (n=6); 2, *Lemur macaco* (6); 3, *Lemur catta* (6); 4, *Propithecus verreauxi* (6); 5, *Daubentonia madagascariensis* (2); 6, *Hapalemur griseus* (8); 7, *Phaner furcifer* (2); 8, *Lepilemur mustelinus* (6); 9, *Avahi laniger* (4); 10, *Cercopithecus nictitans* (6); 11, *Cebus apella* (6); 12, *Galago crassicaudatus* (6); 13, *Aotus trivirgatus* (6); 14, *Callicebus moloch* (24); 15, *Perodicticus potto* (6); 16, *Nycticebus coucang* (7); 17, *Nycticebus pygmaeus* (5); 18, *Cheirogaleus major* (4); 19, *Loris tardigradus* (6); 20, *Callithrix jacchus* (6); 21, *Tarsius syrichta* (6); 22, *Galago senegalensis* (6); 23, *Microcebus murinus* (6). Data from ref. 7.

embryo, and the ethmoid appears in the medial orbital wall of the adult.

Primates with an os planum are either small animals with relatively large eyes (as a result of negative allometry), or animals with pronounced orbital convergence, or both (Fig. 1). With increase in body size and consequent decrease in relative eye size, orbit and nasal fossa "compete" less for the available cranial volume, and the ethmoid may disappear again beneath laminae of the periorbital membrane bones. This sometimes happens in large gorillas⁵, and may have occurred in the evolution of larger Madagascar primates from *Microcebus*-sized ancestors. If the last common ancestor of the extant primates was a small animal with large and convergent orbits, it probably had an ethmoid component in the medial orbital wall. It seems as likely that *Daubentonia*, *Phaner*, the lemurs and the indriids have lost the os planum independently, as that *Microcebus*, *Cheirogaleus*, *Tarsius*, the Lorisiformes and the anthropoids have acquired it independently. Although *Necrolemur* is said to lack an os planum, the medial orbital wall of *N. antiquus* as reconstructed by Simons and Russell⁶ strongly resembles that of an adult *Microcebus* after the disappearance of the frontoethmoidal suture⁴; a distinct os planum may well have been present in juvenile *Necrolemur*.

MATT CARTMILL

Departments of Anatomy and Sociology-Anthropology,
Duke University,
Durham, North Carolina 27706

¹ Szalay, F. S., *Nature*, **230**, 324 (1971).

² Forsyth Major, C. I., *Proc. Zool. Soc. Lond.*, **1**, 9 (1901).

³ Jones, F. W., *Proc. Zool. Soc. Lond.*, **1**, 323 (1917).

⁴ Kollman, M., *Mém. Soc. Linn. Normandie (Zool.)*, NS **1**, 1 (1925).

⁵ Bolck, L., *Verh. K. Akad. Wet.*, Amsterdam, 2 sectie, **20** (5), 1 (1919).

⁶ Simons, E. L., and Russell, D. E., *Breviora*, **127** (1960).

⁷ Cartmill, M., thesis, Univ. Chicago (1970).

Is Vertesszöllös II an Occipital of European *Homo erectus*?

THE taxonomy of the two human fossils discovered at the Intermindel occupation site of Vertesszöllös in western Hungary has been a topic of considerable interest. The fragments of a deciduous tooth representing the first individual (V1) were judged by Thoma to be indistinguishable from deciduous teeth from Choukoutien¹, but he later concluded that the second individual (V2), represented by an occipital fragment, is a member of the taxon *Homo sapiens*^{2,3}. He places V2 on the lineage leading to Swanscombe, in preference to separate lineage leading to the neandertals.

The "chopper-chopping tool" industries at Vertesszöllös and at Choukoutien are quite similar⁴, which leads to the somewhat bizarre conclusion that two different hominid species are associated with a chopper-chopping tool industry at Choukoutien (*Homo erectus*) and at Vertesszöllös (*Homo sapiens*), and the same two species are associated with a hand axe industry at Ternifine (*Homo erectus*) and Swanscombe (*Homo sapiens*). Because the industry at Vertesszöllös is, for all intents and purposes, the same as that at Choukoutien where *Homo erectus* material from the same time period has been found⁵, and because Thoma convincingly demonstrated that V1 cannot be distinguished from this *Homo erectus* sample¹, it is of some interest to examine his basis for placing V2 in *Homo sapiens*^{2,6}.

In his most recent analysis, Thoma concludes² that "the majority of gross morphological features of Vs. 2 is Archaic in character". Most of these features are characteristic of *Homo erectus*^{7,8}, and measurements of thickness are completely within the *Homo erectus* range, usually falling between the values for the material from Peking and Java. Theinion angle of the occipital is quite low. The nuchal torus is heavy, and extends laterally across the entire bone in the fashion of almost every other *Homo erectus* specimen, and unlike australopithecines, neandertals, modern men, and the other early European specimens—Swanscombe and Steinheim. The torus is quite high. Theinion is considerably higher than the internal occipital protuberance which indicates the extent of the nuchal musculature, and suggests that the individual was large and probably male. The total morphological pattern is far more similar to a large *Homo erectus* than it is to a large neandertal. The two other early European crania are later, and are possibly female. Comparisons are therefore misleading.

In contrast, there are few reasons for placing the occipital in *Homo sapiens*, Thoma's *Paläanthropus* grade. Thoma claims only two: a high and fairly curved profile of the upper part of the occipital squama projected in the sagittal plane, and a cranial capacity significantly greater than *Homo erectus*. The sagittal curvature of the upper part of the squama is indicated by the index of the lambda-inion arc to the lambda-inion chord. In V2 this index is 108.2; a sample of nine *Homo erectus* specimens average 105 and range from 102.3 to 108.4 (s.d. = 1.8).

The high profile of the upper part of the squama is misleading, for the angle at the inion is not particularly great. Its value, 103°, is equal to or less than those of almost every occipital in the Peking group, and is considerably smaller than the angle in Swanscombe (118°), a more recent European specimen. The upper squama matches Peking crania such as 10 quite well in sagittal profile, except for the fact that it extends more anteriorly, and consequently is higher. There are, however, wormian bones in the vicinity of lambda which make it impossible to determine exactly where lambda is. Thoma chose the most anterior point, whereas Martin suggests⁹ the point where lines smoothly approximating the course of the lambdoidal suture cross each other. This point is more posterior, and consequently lower, in the V2 occipital. Use of the proper point would diminish the two chords which now fall outside the *Homo erectus* range by being too large, lambda-inion and lambda-opisthion.

Table 1 Comparison of Regression Parameters, Fit and Correlation for Lambda-Opisthion Chord and Cranial Capacity

		Slope	Intercept	Correlation	Percentage error of regression fit	Sample size
<i>Homo erectus</i>	(1)	23.77	-1,052.4	0.95	3.6	5
	(2)	22.30	-910.7	0.89	4.1	7
Neandertals		22.36	-1,344.3	0.82	6.4	14
<i>Homo sapiens</i>		25.71	-1,047.7	0.83	5.8	200

Table 2 Calculation of *Homo erectus* Cranial Capacities by Regression with the Lambda-Opisthion

Specimen	Lambda-opisthion chord (mm)	Actual cranial capacity (cm ³)	Calculated cranial capacity by regression		
			Wolpoff (n=5)	Wolpoff (n=7)	Thoma
Java	(1)	78 *		822	877
	2	75		753	797
	4	78	731	822	877
	6	81 *	802	891	957
Peking	3	84		960	1,037
	11	86		1,006	1,090
	12	87		1,029	1,117
Average absolute difference			32	37	68
Percentage difference			4%	4%	8%
Calculated Vertesszöllös capacity			1,325	1,328	1,463

* Estimated.

Thoma estimates the cranial capacity of V2 by means of a regression equation^{2,6} which relates the lambda-opisthion chord to cranial capacity. Of the twelve specimens used by him, only five were *Homo erectus*, and with these he mixed five Solo crania and the Swanscombe and Broken Hill specimens. He conservatively uses the lower 95% confidence limit and concludes that the capacity must be greater than 1,400 cm³, using his lambda-opisthion measure of 102 mm, or greater than 1,350 cm, using Tobias's measure of 100 mm.

I have calculated separate regressions for *Homo erectus*, neandertals, and 200 *Homo sapiens* specimens chosen at random from publications in *Biometrika*. Of the seven available specimens of *Homo erectus*, the positions of opisthion were uncertain in Java 1 and 6 and have been estimated in the literature. Regressions were calculated for the *Homo erectus* sample both with and without these specimens. The equations and correlations are given in Table 1.

The correlation for the regression using the small (unestimated) *Homo erectus* sample alone is greater than Thoma's correlation of 0.93 for his entire sample. The correlation value for the neandertals is lower, but this calculation used all of the published neandertal measurements (n=14), instead of only a few (n=6).

Table 2 indicates a test of the regressions by predicting the known cranial capacities in the *Homo erectus* sample. The percentage error for *Homo erectus* both with and without the two questionable specimens is close to 4%, but the percentage error of Thoma's equation when used to predict capacities only for *Homo erectus* is twice as great. The percentage error of Thoma's equation used to predict only the five specimens for which opisthion is known is greater still; almost 10%.

The archaeological evidence, the morphology of VI from the same site and by Thoma's admission most features of V2 suggest that the specimen is *Homo erectus*. It thus seems reasonable to use a regression based on *Homo erectus* specimens to estimate its cranial capacity. The regression for either sample gives almost identical estimations for V2, using Tobias's value of 100 mm for the lambda-opisthion chord. Because the actual value of the chord may be less, the estimation of about 1,325 cm³ is a maximum.

Is the capacity of V2 large enough to be outside of the expected range of *Homo erectus* variation? The 95% range

cannot be used because it is too large to be meaningful (± 345 cm³). The estimate is only 100 cm greater than the Peking 10 capacity. A *t* test comparing V2 with a sample of cranial capacities¹⁰ of twelve *Homo erectus*, excluding the V2 value itself, indicates that V2 is not significantly different from *Homo erectus* on the 5% level. Along with all of the Peking crania, the capacity is, of course, within the range of variation for *Homo sapiens*.

In sum, it seems likely that V2 is the occipital of a *Homo erectus*. V2's similarity to the Swanscombe material is not surprising in view of the strong possibility that the English cranium is a member of the same lineage somewhat later in time.

M. H. WOLPOFF

Department of Anthropology,
University of Michigan,
Ann Arbor,
Michigan 48104

Received March 15; revised May 4, 1971.

- 1 Thoma, A., *Z. Morphol. Anthropol.*, **58**, 152 (1967).
- 2 Thoma, A., *Z. Morphol. Anthropol.*, **60**, 229 (1969).
- 3 Thoma, A., *Yb. Phys. Anthropol.*, **13**, 137 (1965).
- 4 Kretzoi, M., and Vertes, L., *Curr. Anthropol.*, **6**, 74 (1965).
- 5 Howells, W. W., *Sci. Amer.*, **215** (5), 46 (1966).
- 6 Thoma, A., *L'Anthropologie*, Paris, **70**, 495 (1966).
- 7 Weidenreich, F., *Bull. Geol. Soc. China*, **19**, 479 (1940).
- 8 Weidenreich, F., *Anthrop. Pap. Amer. Mus. Nat. Hist.*, **40** (1945).
- 9 Martin, R., *Lehrbuch der Anthropologie*, vol. 2, *Krainologie, Osteologie*, 614 (Fisher, Stuttgart, 1928).
- 10 Tobias, P. V., *Olduvai Gorge*, **2**, *The Cranium and Maxillary Dentition of Australopithecus (Zinjanthropus) boisei* (Cambridge University Press, 1967).

New Carbon-14 Evidence for Six Hundred Years Old *Canna compacta* Seed

THE longevity of a viable seed of *Canna* considered to be about 550 years old¹⁻³ has been questioned by Godwin⁴. The specimen, enclosed in a *Juglans australis* nutshell forming part of a rattle necklace was collected from tomb 92 in Santa Rosa de

Tastil, Argentina. New carbon-14 dates presented here, on the nutshell and a trash heap, confirm this to be the oldest viable seed known.

Santa Rosa de Tastil is the first archaeological town dated in the Argentine north-west (24° 25' S, 65° 50' W, 2,800 m altitude). In the site were excavated remains of a conglomerate of about 400 dwellings with an evolved network of streets and squares. About 100 tombs and several contemporaneous trash heaps show that occupation was continuous.

The first radiocarbon analysis, on wood charcoal³ collected in heap 1 together with cameloid bones, dated the site as 530±30 yr BP (years before present defined^{5,6} as before AD 1950). Sivori *et al.*^{1,2} reported in 1968 the germination and growth of one of the *Canna* seeds found inside the nutshells. The plant has since been growing healthily^{7,8} and has reached a height of about 2 m. It flowered and was identified as *Canna compacta* Rosc., by H. Fabris at the University of La Plata. The flowers were self fertilized and produced seeds, which were sown. These germinated with fewer geotropic irregularities than their archaeological ancestor^{1,2,7,8}.

The kind of evidence about the age of the seed demanded by Godwin and Willis^{4,9} is the most desirable if reliable dates are to be found for viable seeds. It involves assaying the carbon-14 of germinating seed before the seedling begins to photosynthesize^{4,9}. This is, however, a destructive analysis, requiring early interruption of growth and combustion of the seedling. This was not feasible in the present case: (1) because of the interest in observing the plant growth and eventually determining its species; (2) the organic chemicals used to stimulate germination might have altered the radiocarbon content of the seed by assimilation or by isotopic exchange, and (3) the amount of material—several grammes of carbon—necessary to provide a precise date was not available. The weight of each of the three *Canna* seeds found was about 200 mg. With a yield of carbon only a fraction of the total weight, dating could have been possible only in a "mini-counter"¹⁰. This, however, would have not been useful because of the large standard deviation of such a measurement (1σ =several hundred years; see Fig. 2 of ref. 10).

Fortunately there were two indirect ways of radiocarbon dating the seed: by analysing the nutshell and the charcoal remains. These data could be interpreted on the basis of the archaeological evidence now being documented⁸ by Sivori *et al.*^{1,2}, and summarized here. (1) The ceramics and other remains, such as the bone artefacts and textiles found in tomb 92 associated with the rattle necklace, are of the same style as those found in heap 1; (2) there are no signs of any intrusions or other perturbations in the material accumulated in the trash heap; (3) the seed has to be contemporaneous or older than the *Juglans* nutshell, because the seed could only have been introduced into the nutshell as long as the nut was still unripe. This was done through a slit cut into it, which after hardening contributes to the characteristic sound of the rattle. Similar rattles have been described by Casanova and von Rosen^{11,12}, for pre-Inca sites.

By measuring the carbon-13 content of the samples^{3,19} all radiocarbon analyses were corrected for isotopic fractionation¹³ to avoid errors which could be as much as 250 yr^{14-16,3,17}. The carbon-14 dates obtained in BP were transformed to true, historical or calendar years AD. This conversion was done by means of a calibration curve based on measurements of carbon-14 in tree rings. The ambiguity^{4,18} between the scales BP and AD caused by the fluctuations of the atmospheric content of the isotope can thus be removed. As the curve of Lerman *et al.*¹⁹ based on Argentine samples does not extend further back than 550 yr BP, we used the curve of Stuiver and Suess²⁰ for the Northern Hemisphere, modified to account for the observation that Southern Hemisphere samples seem to be about 40 yr older^{19,21}.

The nutshell was dated as 620±60 BP (GrN-5818)*, converted to AD 1362±73. Heap 1 was divided in seven stratigraphic layers of 20 cm thickness each. Charcoal from layers 1, 4 and 7 was radiocarbon dated: 580±35 BP (GrN-5807), 650±45 BP (GrN-5808), and 635±30 BP (GrN-5809), respectively. These dates and that previously reported³ (530±30 BP (GrN-5147)) also dates layer 1. The converted dates are: AD 1418±19 for layer 1 (weighted average of the two samples); AD 1336±50 for layer 4; AD 1349±41 for layer 7. Our statistical analysis suggests that the accumulation of the whole trash heap took about 90 yr²², and that the longest accumulation period, with a confidence level of 95% (2 σ interval), was AD 1282 to AD 1467 (ref. 22). As we have shown, the rattle as well as the seed were contemporaneous with the trash heap. The antiquity of the nut ranges from AD 1216 to AD 1508 (2 σ interval). The nutshell and the trash heap dates are thus consistent.

The carbon-14 analyses also agree with the dating based on the archaeological and historical chronologies for the region: the excavated potsherds belong to the Late Ceramic Period which dates between AD 1000 and AD 1450, and the absence of Inca objects determines as *terminus ante quem* AD 1450 to AD 1550.

We conclude therefore that the seed from Santa Rosa de Tastil was about 600 yr old when germinated. Compared with documented lists^{4,9,23,24} this is the oldest known viable seed. The resistance of *Canna* seeds to hard treatment has been reported²⁵ (for example, germination of seeds threaded forming a rosary, and of seeds kept about 30 yr in a herbarium).

We are indebted to the Groningen Physics Laboratory for the isotope analyses. This work was begun while J. C. L. was on the staff of that laboratory.

J. C. LERMAN

Physikalisches Institut,
Universität Bern,
3000 Bern, Switzerland

E. M. CIGLIANO

Facultad de Ciencias Naturales y Museo,
Universidad Nacional de La Plata,
La Plata, Argentina

Received October 26, 1970.

- ¹ Sivori, E., Nakayama, F., and Cigliano, E. M., *Nature*, **219**, 1926 (1968).
- ² Nakayama, F., and Sivori, E., *Rev. Fac. Agron. Univ. Nac. La Plata*, **44** (1), (1968).
- ³ Vogel, J. C., and Lerman, J. C., *Radiocarbon*, **11**, 351 (1969).
- ⁴ Godwin, H., *Nature*, **220**, 708 (1968).
- ⁵ Deevey, E. S., Flint, R. F., and Rouse, I., *Radiocarbon*, **5**, v (1963).
- ⁶ Olsson, I. U., in *Radiocarbon Variations and Absolute Chronology* (Proc. Twelfth Nobel Symp.) (Almqvist, Stockholm; Wiley, New York, 1970).
- ⁷ Cigliano, E. M., Lerman, J. C., and Sivori, F., *Actas Thirty-ninth Cong. Intern. Amer. Lima 1970* (in the press).
- ⁸ Sivori, F., and Nakayama, F., in *Santa Rosa de Tastil: una Comunidad Prehispánica* (edit. by Cigliano, E. M.) (in the press).
- ⁹ Godwin, H., and Willis, E. H., *Radiocarbon*, **6**, 132 (1964).
- ¹⁰ Oeschger, H., Alder, B., Loosli, H., and Langway, C. C., *Earth. Planet. Sci. Lett.*, **1**, 49 (1966).
- ¹¹ Casanova, E., *Relac. Soc. Argent. Antrop.*, **3** (1942).
- ¹² von Rosen, E., in *Un mundo que se va*, 123 (1957).
- ¹³ Craig, H., *J. Geol.*, **62**, 115 (1954).
- ¹⁴ Lerman, J. C., in *Radiocarbon Variations and Absolute Chronology* (Proc. Twelfth Nobel Symp.) (edit. by Olsson, I. U.), 104 (Almqvist, Stockholm; Wiley, New York, 1970).
- ¹⁵ Oeschger, H., Riesen, T., and Lerman, J. C., *Radiocarbon*, **12**, 358 (1970).
- ¹⁶ Oeschger, H., and Lerman, J. C., *Bull. Schweiz. Verein. Atomenerg. Beil.*, No. 12, 1 (1970).
- ¹⁷ Goodwin, H., *Amer. J. Bot.*, **57**, 723 (1969).
- ¹⁸ *Radiocarbon Variations and Absolute Chronology* (Proc. Twelfth Nobel Symp.) (edit. by Olsson, I. U.) (Almqvist, Stockholm; Wiley, New York, 1970).
- ¹⁹ Lerman, J. C., Mook, W. G., and Vogel, J. C., in *Radiocarbon Variations and Absolute Chronology* (Proc. Twelfth Nobel Symp.) (edit. by Olsson, I. U.), 275 (Almqvist, Stockholm; Wiley, New York, 1970).

* Laboratory numbers are given in parentheses.

- ²⁰ Stuver, M., and Suess, H. E., *Radiocarbon*, **8**, 534 (1966).
²¹ Lerman, J. C., Mook, W. G., Vogel, J. C., and de Waard, H., *Science*, **165**, 1123 (1969).
²² Lerman, J. C., in *Santa Rosa de Tastil: Una comunidad pre-hispánica* (edit. by Cigliano, E. M.) (in the press).
²³ Godwin, H., and Willis, E. H., *New Phytol.*, **63**, 410 (1964).
²⁴ *Sci. Progrès—La Nature*, No. 3395, 95 (1968).
²⁵ Kränzlin, F., in *Das Pflanzenreich* (edit. by Engler, A.), **4**, No. 47, 16 (Engelmann, Leipzig, 1912).

Isozyme Variation under Selection in *Zea mays*

THE extent of polymorphism in genetically determined isozyme variants (allozyme variation) in natural populations raises the issue of its adaptive significance. It was originally thought that this variation is neutral with respect to fitness¹, but recent evidence supports the assertion that its maintenance involves a selective component². If an allelic substitution yields an enzyme with altered properties³, maintenance by selection in natural populations may result in a distinct geographic distribution of allele frequencies. Such a pattern has been described⁴ in the case of a serum esterase polymorphism in the freshwater fish *Catostomus clarkii*.

Isozyme gene frequencies were examined in a symmetrical set of lines after prolonged selection for and against a specific metabolic property. We did this by assaying enzyme polymorphism in the highly selected strains of maize from the breeding experiment established by Hopkins⁵. From 163 open-pollinated ears of the local maize variety Burr White, he set up four strains (HO, LO, HP and LP) which were selected for high and low seed levels of oil and protein respectively. The long term responses to selection in these Illinois strains are now considered classic examples in both evolutionary theory⁶ and plant breeding⁷. Reverse selection⁸ has displayed considerable genetic variance persisting after forty-eight generations, and variance analysis⁸ after sixty-five generations. Thus, a comparison of electrophoretic variants in these strains may provide a test of whether isozyme variants are selectively neutral.

Seedlings of the four directional strains (HO, LO, HP and LP) and Leng's four reversed strains (RHO, RLO, RHP and RLP) were assayed for E_1 , E_3 , E_4 and E_{12} (esterases), alcohol dehydrogenase (*Adh*) and peroxidase (*Px*) by techniques described before⁹. Twenty generations of selection have elapsed since the four reverse lines were isolated⁵ in 1948. Sample size exceeded fifty seedlings except for LO of which there were only thirty because it germinated poorly. The gene frequency estimates (Table 1) show that each of the eight strains is genetically distinct. More than two strains are polymorphic for each locus: the *S* and *N* alleles at the E_1 and *Px* loci and the *S* and *F* alleles at the E_3 , E_{12} , *Adh* and E_4 loci, while the low protein (LP) strain was polymorphic for the *S* and *N* alleles at the E_4 locus.

Table 1 Gene Frequency Estimates of the Slow (*S*) Allele for Six Isozyme Loci in Eight Selected Strains of Maize

Selected strain	E_1	E_3	E_4	E_{12}	<i>Adh</i>	<i>Px</i>
Oil content						
High (HO)	0.93	1.00	0.00	0.29	0.33	0.00
Low (LO)	0.57	0.00	1.00	0.83	0.04	1.00
Reverse high (RHO)	0.14	0.76	0.50	0.15	0.29	0.51
Reverse low (RLO)	0.14	0.00	0.34	1.00	0.00	0.23
Protein content						
High (HP)	0.00	0.49	1.00	0.00	0.00	0.50
Low (LP)	1.00	0.00	0.30*	0.00	0.00	0.00
Reverse high (RHP)	0.00	0.18	1.00	0.00	0.74	0.81
Reverse low (RLP)	0.28	0.00	1.00	0.00	0.15	0.12

* Polymorphic for the *S* and *N* alleles.

The mating design of the experiment⁵ has enforced out-crossing between selected ears within a strain. To test for the Hardy-Weinberg genotypic distribution, estimates of the fixation index were made for each variable locus in each strain. The fixation index (*F*) is a measure of the proportionate deficiency of heterozygotes at census, and absolute values of *F* greater than $1.96/N^{1/2}$ ($=0.28$) are required to reject the null hypothesis¹⁰ that $F=0$. The values shown in Table 2 conform to the Hardy-Weinberg distribution.

Table 2 Fixation Index Estimates for Six Isozyme Loci in Eight Selected Strains of Maize

Selected strain	E_1	E_3	E_4	E_{12}	<i>Adh</i>	<i>Px</i>
Oil content						
High HO	-0.08	—	—	0.10	-0.07	—
Low LO	-0.24	—	—	-0.21	-0.05	—
Reverse high RHO	-0.03	0.18	0.06	-0.02	-0.09	0.03
Reverse low RLO	-0.17	—	-0.11	—	—	-0.02
Protein content						
High HP	—	-0.21	—	—	—	0.06
Low LP	—	—	-0.03	—	—	—
Reverse high RHP	—	-0.08	—	—	-0.07	-0.11
Reverse low RLP	0.13	—	—	—	-0.18	-0.14

Selection of twelve ears per strain in this design reduces the effective population size (N_e) to no less than thirty individuals. Assuming that by 1948 the rate of neutral fixation of loci had reached the steady state ($1-1/2N_e$) of variable loci would remain unfixed after each generation. Therefore $(59/60)^{20} \approx 0.7$ of the variable neutral loci in 1948 would remain unfixed after twenty generations.

Consider the hypothesis that all the allozymic differentiation among the strains is attributable to genetic drift. The following points argue in favour of this hypothesis. First, half of the twelve comparable results at specific loci in Table 1 do not directly correspond to directionally consistent changes. For example, the E_1^s allele is less frequent in the reverse low oil (RLO) strain than in the low oil (LO) strain, whereas it is most frequent in the high oil (HO) strain. Second, when reverse selection began, there were at least eighteen loci still variable because eighteen of the twenty-four paired comparisons between the current forward and reverse strains are dissimilar. Of these, twenty-four out of thirty-six remain unfixed in the current generation, and this proportion agrees well with that predicted by drift.

Yet other observations suggest that a selective component may be superimposed. First, of the twelve fixations occurring in the last twenty generations, nine were fixed under forward and only three under reverse selection (one-tail probability of 0.07). Second, the assumption of the steady state and the minimal estimate of N_e have probably inflated the estimate of the effect of drift in these strains. And Table 1 shows that while on average the reverse selection strains vary at more loci than the forward strains (a mean of 3.75 c.f. 2.25), the same difference occurs between the oil strains as a group and the protein strains. Such biases could arise from selective rather than neutral fixation.

These results are acceptable on the hypothesis of purely neutral drift but the deviations suggest that isozyme variants are not entirely neutral to selection.

I thank Drs J. W. Dudley and D. E. Alexander for seeds and Dr J. R. G. Turner and Professor M. H. Williamson for discussion.

ANTHONY H. D. BROWN

Department of Biology,
University of York

Received March 9; revised May 10, 1971.

¹ Shaw, C. R., *Science*, **149**, 936 (1965).

² Richmond, R. C., *Nature*, **225**, 1025 (1970).

- ³ Gibson, J., *Nature*, **227**, 959 (1970).
⁴ Koehn, R. K., *Science*, **163**, 943 (1969).
⁵ Leng, E. R., *Z. Pflanzenzucht*, **47**, 67 (1962).
⁶ Stebbins, *Processes of Organic Evolution* (Prentice Hall, New Jersey, 1966).
⁷ Allard, R. W., *Principles of Plant Breeding* (Wiley, New York, 1963).
⁸ Dudley, J. W., and Lambert, R. J., *Crop. Sci.*, **9**, 179 (1969).
⁹ Brown, A. H. D., and Allard, R. W., *Crop. Sci.*, **9**, 72, 634 (1969).
¹⁰ Brown, A. H. D., *Genetica*, **41**, 399 (1970).

Shrub Ecotypes in a Salt Desert

A SALINITY gradient extends from the highly saline beaches of the Great Salt Lake of Utah to the surrounding non-halomorphic soils, with a correlated vegetation gradient in which a succession of plant communities grows in concentric zones. The chief communities, in decreasing order of soil salinity, are dominated by (1) *Salicornia-Allenrolfea*; (2) *Sarcobatus vermiculatus*; (3) *Atriplex-Eurotia*; and (4) *Artemisia tridentata*¹. Within these communities are perplexing local distributions of co-dominant species. Typical communities within the *Atriplex-Eurotia* zone include pure *Atriplex confertifolia*, *Atriplex-Eurotia*, pure *Eurotia lanata*, *A. confertifolia* *Artemisia spinescens-Eurotia* grass, and pure *Atriplex nuttallii*. Although these communities are separated by sharp ecotones, local soil variations are insufficient to explain the distribution of the different plant communities².

We have investigated first, the possibility that genetic differences between local populations of *A. confertifolia* and *E. lanata* explain their distribution in or near the five communities within the *Atriplex-Eurotia* zone. Second, we investigated the contribution of genetic differences to the wide tolerance to salinity shown by *A. nuttallii*, which occurred locally in pure stands along the whole salt gradient. Populations of *A. nuttallii* were sampled from the *Salicornia-Allenrolfea* zone, from two communities in the *Sarcobatus* zone, and from the *Atriplex-Eurotia* zone in Curlew Valley, north of the Great Salt Lake.

Sample plants of *A. confertifolia* and *E. lanata* from within the *Atriplex-Eurotia* zone, and of *A. nuttallii* along the salt gradient were removed in blocks of native silt with minimal root damage, and were grown for at least 6 weeks in a glass-house. Initial soil conductivities were recorded (Table 1). The plants were then grown at 27° C with a 16 h photoperiod in nutrient culture³ with high levels of salt (10 mM) and boron (0.1 mM) to simulate the average soil condition. Concentrated sodium nitrate solution (16.5 mM) was added to increase plant growth rate. These cultures had conductivities of approximately 50 mmho.

Three measurements were made on six plants from each site in November 1970. These were (a) mean shoot dry weight increase in 3 weeks ($\bar{W}_s$); (b) relative leaf growth rate⁴ ($\bar{R}_L$), and (c) nitrate reductase activity ($\bar{A}_N$)⁵. These were chosen as representing different levels of expression of plant activity.

Plants of *E. lanata* from the *Atriplex-Eurotia* zone had a large yield and a very active nitrate reductase system, but variability between populations in these parameters was small (Table 1). On the other hand, populations of *A. confertifolia* demonstrated marginally significant ($P=0.05$) differences in both yield and nitrate reductase activity between sites. The pure stand (P) plants had the lowest dry weight increase, whereas the *A. nuttallii* site (N) plants had lowest nitrate reductase activity. This implies that genetic differences did exist between the different populations of *A. confertifolia*. This species is dioecious with vegetatively distinct sexes, and it was also found that female plants yielded more than males ($P<0.05$).

Populations of *A. nuttallii* from along the salt gradient demonstrated significant differences ($0.05 > P > 0.001$) in all

parameters (Table 1). Further, plants of *A. nuttallii* from the *Atriplex-Eurotia* zone had distinctly smaller leaves than the other populations. In the other sites, R, K and S (Table 1) *A. nuttallii* appeared to be morphologically uniform. Several subspecies, or possibly true species, have been described within the *A. nuttallii* complex⁶, so that the distinct morphology and physiology of the plants in the *Atriplex-Eurotia* zone may indicate that they should be accorded subspecific status.

In spite of the large variation in soil conductivity within the *Sarcobatus* zone (Table 1), its two *A. nuttallii* populations (R and K) did not differ significantly. The *A. nuttallii* population from the *Salicornia-Allenrolfea* zone, however, was lower in yield, leaf growth rate and nitrate reductase activity than in the *Sarcobatus* zone plants. Three distinct populations of *A. nuttallii* therefore existed along the salt gradient, which may account for the wide salt tolerance of this species.

Table 1 Soil and Yield Characters of Three Salt Desert Species

Site	<i>E. lanata</i>				<i>A. confertifolia</i>			
	Soil conductivity	$\bar{W}_s$	$\bar{R}_L$	$\bar{A}_N$	Soil conductivity	$\bar{W}_s$	$\bar{R}_L$	$\bar{A}_N$
Pure stand (P)	0.8	18	0.35	235	10	8	0.15	35
<i>Atriplex-Eurotia</i> (M)	0.8	15	0.25	260	0.8	12	0.35	48
Near <i>A. nuttallii</i> (N)	1.4	16	0.15	278	1.4	16	0.37	11
<i>Atriplex-A. spinescens-Eurotia</i> grass (G)	1.0	18	0.18	272	1.0	12	0.37	82
SE	—	3.4	0.08	43	—	1.8	0.10	22

Site	<i>A. nuttallii</i>			
	Soil conductivity	$\bar{W}_s$	$\bar{R}_L$	$\bar{A}_N$
<i>Atriplex-Eurotia</i> zone (N)	1.4	10	0.39	29
<i>Sarcobatus</i> zone (R)	5.2	17	0.60	106
<i>Sarcobatus-Suada</i> (K)	96	21	0.60	173
<i>Salicornia-Allenrolfea</i> zone (S)	121	14	0.42	9
SE	—	3.2	0.05	24

Soil conductivity is given in mmhos; $\bar{W}_s$, dry weight (mg) per shoot; $\bar{R}_L$, relative leaf growth rate; $\bar{A}_N$, nitrate reductase activity (mM NaNO_2/g fresh weight/h).

The variation in nitrate reductase activity as well as in yield and leaf growth rate in *Atriplex* but not in *Eurotia* suggests that in *Atriplex*, as in the Gramineae⁶, nitrate reductase activity may be inherently variable. All of the three parameters were sufficiently variable to indicate considerable genetic variation in the *Atriplex* species studied. This contrasts with the finding of Hannon and Bradshaw⁷ who reported that two co-existing maritime grasses were in a similar state of evolutionary adaptation to salinity. Our work suggests that these three desert chenopods, *A. confertifolia*, *E. lanata* and *A. nuttallii*, differ considerably in their state of evolutionary diversification. Indeed, the observation of interspecific hybridization in *A. nuttallii*⁵ indicates that this species is in a very active state of evolution, and this probably accounts for its wide distribution.

Investigations are continuing with clones of the different populations growing in different environments (particularly different salinities) to test the adaptive nature of the population differences. This work and the possibility of genetical experiments in the future, however, is limited by the slow growth of woody *Atriplex* clones.

This investigation was carried out at Utah State University with the aid of grants from the Ecology Center, the Utah

Agricultural Experiment Station, the US/IBP Desert Biome and the British Agricultural Research Council.

P. J. GOODMAN

Welsh Plant Breeding Station,
Plas Gogerddan,
Aberystwyth

M. M. CALDWELL

Range Science Department and
The Ecology Center,
Utah State University,
Logan,
Utah 84321

Received February 8; revised May 18, 1971.

- ¹ Flowers, S., and Evans, F. R., in *Salinity and Aridity* (edit. by Boyko, H.), 367 (W. Junk, the Hague, 1966).
- ² Gates, D. H., Stoddart, L. A., and Cook, C. W., *Ecol. Monog.*, **26**, 155 (1956).
- ³ Bowerman, A. E., and Goodman, P. J., *Ann. Bot.* (in the press).
- ⁴ Watson, D. J., *Ann. Bot.*, **22**, 37 (1956).
- ⁵ Hanson, C. A., thesis, Brigham Young University (1962).
- ⁶ Beevers, L., and Hageman, R. H., *Ann. Rev. Plant Physiol.*, **20**, 495 (1969).
- ⁷ Hannon, N., and Bradshaw, A. D., *Nature*, **220**, 1342 (1968).

Flow of Red Blood Cells stopped by Ultrasound

ULTRASOUND has applications in physiotherapy in the treatment of musculoskeletal disorders¹, and recent findings indicate a potential value as a local anabolic agent²⁻⁴. It is used to detect tumours⁵ and fetuses⁶, while a further application lies in measuring the rate of blood flow in terms of corpuscular velocity^{7,8}. The increasing use of ultrasound on human tissues has led to concern for possible hazards. It is essential that safety limits are determined accurately and that the interactions of ultrasound with living tissues are investigated so that they can be predicted when ultrasound is used within these limits. Largely in this connexion, we are investigating the effects of low intensity ultrasound on blood circulation in living tissues and wish to report a striking finding: the aggregation of red blood cells into stationary clumps in the radiation field (Fig. 1).

A chick embryo at the 3.5 day stage of incubation, together with its extra-embryonal membranes, was dissected free from the yolk in such a way as to keep the sinus terminalis intact, and placed in a saline-filled irradiation chamber⁹ maintained at 37° C by a heated microscope stage, and consisting of a shallow rectangular metal tray fitted with a strip transducer at one of the shorter ends. The wall at the end opposite the transducer could be faced with either a reflector or with various combinations of absorbing materials. There was a central viewing area of thin glass over which the embryo was placed with its attached extra-embryonal membranes lightly stretched. The heart beat continued apparently normally for several hours in this preparation. The flow of red cells through the vessels of the chick and its associated membranes were viewed with a light transmission microscope. The ultrasonic field was monitored by a small, sensitized, thermistor probe which could be positioned at any point in the radiation field by means of a micromanipulator attached to the irradiation chamber.

We found that when particulate matter was suspended in the saline it aggregated into clumps arranged in vertical planes at right angles to the direction of propagation of the ultrasound. These aggregates were spaced at half wavelengths throughout

the field. When the embryo was placed in the chamber, we found that above certain threshold intensities the blood cells in the developing vessels aggregated in a similar manner, and in some cases circulation was arrested. Red cell stasis was temporary, for the clumps broke down when irradiation ceased.

So far we have used only continuous 3 MHz irradiation. Threshold intensities for red cell aggregation are apparently determined by the nature of the vessel. When the ease of aggregation is compared in adjacent arteries and veins of similar bore, the threshold intensity is significantly lower in the vein than in the artery ($d = -1.22$, $N = 9$, $t = -5.8568$, $P < 0.0005$). Red cell stasis occurred more readily in large bore veins than in those of small bore. In arteries near the heart the situation was more complex because the red cell clumps are affected by pressure changes at each heart beat.



Fig. 1 Surface view of the area vasculosa of a chick embryo at the 3.5 day stage of incubation demonstrating ultrasonically induced red cell stasis ($\times c. 26$).

When stasis was complete red cell aggregates were sharp-edged (Fig. 1). In conditions producing incomplete stasis, red cells could be seen breaking away from the downstream edges of the bands only to be trapped at the upstream edge of the next band. When irradiation ceased each band assumed the parabolic profile typical of Poiseuille flow before dissolution was complete (Fig. 2).

The fact that the aggregates were sharp-edged suggests that the red cells were not held together simply as a result of standing wave formation. We consider that Bernoulli attractions may be involved. If reflexion played a more important role in aggregate formation than simply determining the position of the aggregates in the radiation field, then one would expect a continuous gradation in red cell density between adjacent aggregates rather than the sharp limits that we have found. Other evidence also suggests that reflexion is a minor component of the forces producing aggregation. Masking the terminal reflector, the wall of the chamber opposite the transducer, by putting an absorber in front of it, did little to affect the threshold intensities required to produce aggregation. When the chamber was replaced by a tank lined by absorbers in which reflexion was minimal, linear aggregation of the red cells in the blood vessels still occurred. These results are interesting because they indicate that a strong reflected wave, such as might be obtained in medical ultrasonic usage at the interface between a soft tissue and air or bone, is not essential for the production of red cell stasis. It seems that only a minor change in acoustic impedance between one tissue and another is sufficient to trigger off the response.

The direction of the blood vessel, relative to the direction of propagation of the ultrasound, is also important in determining the effect on red cell motion. If the vessel is aligned parallel to the ultrasonic field stasis is readily evoked. If the vessel is at right angles to it then the red cells continue to flow within the cell aggregates.

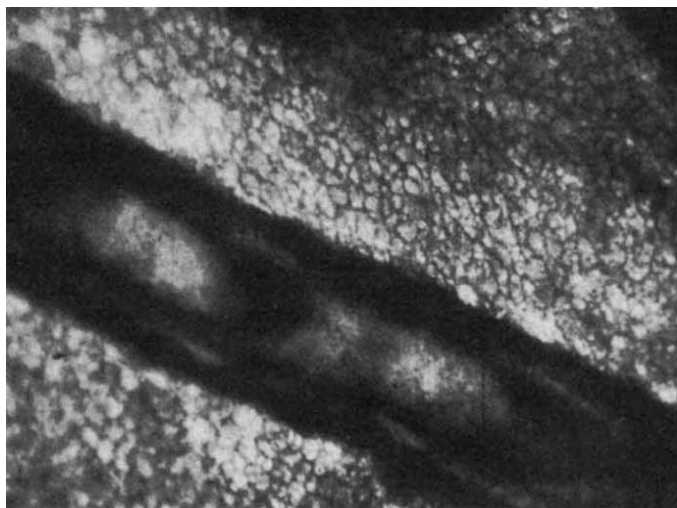


Fig. 2 Parabolic profile of dissociating red cell aggregates in a vein ($\times c. 186$).

One serious effect of red cell stasis in arteries and arterioles is that the tissues supplied by them will be exposed to conditions of reduced oxygen availability. We suggest that this can be minimized by moving the treatment head during ultrasonic irradiation so that the direction of the vessels relative to the direction of propagation of the ultrasound is continuously varied. When this is not possible then the dose parameters should be kept below those producing red cell stasis in the major vessels. We also suggest that the possibility of interference with red cell flow be considered when Doppler probes are used to monitor the circulation of the blood.

We thank Mr Kevin Fitzpatrick and the Department of Medical Photography for assistance with photography, the Medical Research Council and the Wellcome Trust for financial assistance, and Professor R. Warwick for advice and encouragement.

MARY DYSON
B. WOODWARD
J. B. POND

Anatomy Department,
Guy's Hospital Medical School,
London Bridge SE1

Received April 13; revised June 7, 1971.

- ¹ Summer, W., and Patrick, M. K., *Ultrasonic Therapy, a Textbook for Physiotherapists* (Elsevier, London, 1964).
- ² Dyson, M., Pond, J. B., Joseph, J., and Warwick, R., *Clin. Sci.*, **35**, 273 (1968).
- ³ Dyson, M., and Pond, J. B., *Physiotherapy*, **56**, 136 (1970).
- ⁴ Dyson, M., Pond, J. B., Joseph, J., and Warwick, R., *IEEE Trans. Sonics and Ultrasonics*, SU-17, 133 (1970).
- ⁵ Holmes, J. H., *Prog. Clin. Cancer*, **3**, 135 (1967).
- ⁶ Donald, I., *Brit. Med. Bull.*, **24**, 71 (1968).
- ⁷ Rushmer, R. F., Baker, D. W., and Stegall, H. F., *J. Appl. Physiol.*, **21**, 554 (1966).
- ⁸ Gosling, R. G., King, D. H., Newman, L., and Woodcock, J. P., *Ultrasonics for Industry, Conference Papers*, 16 (Iliffe, Guildford, 1969).
- ⁹ Pond, J. B., Woodward, B., and Dyson, M., *Physics Med. Biol.*, **16**, 521 (1971).

Defence and Territorial Behaviour dissociated by Hypothalamic Lesions in the Rat

It has been pointed out that much of the literature on brain mechanisms of aggression fails to distinguish between different kinds of aggressive behaviour, and that this may account for some of the apparent contradictions in different publications¹. In the experiments reported here the effects of hypothalamic lesions were measured on two different types of aggressive behaviour: defence behaviour, which consists of a defensive upright posture and boxing in the shock box; and territorial behaviour, which consists of the offensive side posture and the full attack posture with biting and kicking by a socially isolated home rat against an intruder. These postures associated with social interactions are quite stereotyped in the rat. They are also present in modified form in other rodents and have been illustrated and catalogued previously².

We used adult male hooded rats, raised in the laboratory. Fighting in response to foot-shock (defence behaviour) was elicited by placing a pair of rats in a 'Plexiglas' cage 20 $\times$ 15 cm with an electrified grid floor. Each trial consisted of a series of twenty 60 cycle a.c. shocks lasting 0.5 s and delivered once every second. A grid scrambling device was used to guarantee that the rats could not escape the shock by standing on certain pairs of grids. Fighting threshold was determined by the titration method; that is, shock intensity was raised in a trial after one in which the rats did not fight and was lowered after one in which they did fight. Fighting was defined as defensive upright posture and boxing by both rats in the pair. Among normal rats these were the predominant responses seen, although at high shock intensities the rats sometimes bit at each other or leapt and rolled over together biting and kicking. Behaviour similar to the offensive side posture and full attack posture was not exhibited by normal rats in the shock box.

Territorial behaviour was obtained from rats that had been socially isolated for at least 1 week in a large home cage (1.4 m² of space on six levels with connecting ramps). Fighting, defined as offensive side posture and/or the full attack posture with biting, was exhibited against a male intruder placed in the home cage. The behaviour was quantified by determining the number of minutes in which fighting occurred during the 10 min period after the first occurrence. If no fighting occurred after 30 min, the trial was terminated.

All pairs of rats tested in the shock box showed rearing and boxing. Some rats did not fight off an intruder in the territorial experiment, however, and they were not used in the study.

Testing a rat in the shock box inhibited it from showing territorial fighting characteristics in the home cage. The rat seemed to become conditioned in the shock box to expect pain when approached by another rat. For this reason, the experimental animals were not tested pre-operatively in the shock box, but only after the initial post-operative tests had been carried out in the territorial situation. Post-operative results in the shock box were compared only with results in normal controls.

Lesions were placed in the hypothalamus by stereotaxic procedure using a radio frequency lesion maker. Surgery was performed aseptically on animals anaesthetized with 'Nembutal' (60 mg kg⁻¹) and the rats were allowed 3 days for recovery before behavioural testing. Lesions involving the lateral hypothalamus abolished spontaneous feeding, in which case the animals were maintained by stomach tube feeding. Lesions were assessed on cresyl violet stained serial frozen sections.

Only rats with symmetrical lesions were included in the study. The experimental results (Fig. 1) depended on whether the lesion substantially destroyed the medial hypothalamus (six rats), the lateral hypothalamus (six rats) or both (six rats). The lesions were not confined to one particular structure, but

lateral lesions always interrupted most of the medial forebrain bundle bilaterally. Medial lesions always destroyed the posterior hypothalamus and made substantial invasions at least into the dorsomedial hypothalamus and the posterior portion of the ventromedial nucleus.

This work was supported by a USPHS Biological Sciences training grant.

DAVID B. ADAMS

Department of Psychology,
Wesleyan University,
Middletown,
Connecticut 06457

Received November 3, 1970; revised March 22, 1971.

¹ Moyer, K., *Comm. Behav. Biol.*, 2, 65 (1968).

² Grant, E., and Mackintosh, J., *Behaviour*, 21, 246 (1963); Barnett, S., in *The Rat: A Study in Behaviour*, 81 (1963).

Visual Sensations Produced by Cosmic Ray Muons

IN 1961, D'Arcy and Porter¹ demonstrated that when single cosmic ray muons passed through the eyes of supine, dark-adapted observers, a small proportion produced a detectable visual sensation. The effect was ascribed either to the production of Cherenkov light in the eye media by the relativistic, singly charged particles or to some form of direct stimulation of the retina. Interest in the possible visual effects produced by fast charged particles has revived recently, following reports by the Apollo astronauts that they saw "flashes of light" while in translunar flight; these flashes may have been caused by the action of cosmic ray nuclei on the eyes².

We now present the preliminary results of a study which confirms and extends the observations of D'Arcy and Porter. Cosmic ray muons travelling downwards within roughly 15° of the vertical were selected by a counter telescope consisting of one or two 2.5 cm diameter disks of plastic scintillator and a 58 cm diameter tank of liquid scintillator placed approximately 90 cm below. The observers lay with their heads between the scintillators comprising the telescope. Four body positions were used, to allow study of the effects of muons passing in different directions through the eyes and head. For the prone or supine positions two small scintillators were used, placed in close proximity to each eye. Alternatively, the observers lay on their sides with their visual axes horizontal and a single small scintillator positioned close to the head to select muons passing laterally through either both eyes or through the visual cortex. In each position, a muon detected by the counter telescope actuated a scaler and a loudspeaker to give a click audible to the observer. A higher rate of muons was detected by a second control telescope some distance from the observer; this triggered a second scaler and gave an identical click on the loudspeaker. The observer was simply required to state "yes" or "no" according to whether he saw a flash of light of any character occurring in coincidence with a loudspeaker click. His replies were recorded by an operator who also read the scalers and thus knew whether the muons had passed through the "genuine" or "control" telescopes. The experiment thus consisted of determining whether a higher proportion of affirmative responses was given for those muons which passed through the eyes or cortex as compared with those that passed through the control telescope.

Ten observers each underwent four recording sessions in each of the four body positions; a recording session consisted of 30 min of dark-adaptation followed by 30 min of responses. Our observers, like those of D'Arcy and Porter, differed considerably in their ratios of affirmative replies and for brevity we present in Table 1 the summed responses for all the observers, that is for a total of 20 h of actual observation in each position. *P* represents the probability by a χ^2 test that the yes/total ratios for the genuine and control events came from the same population.

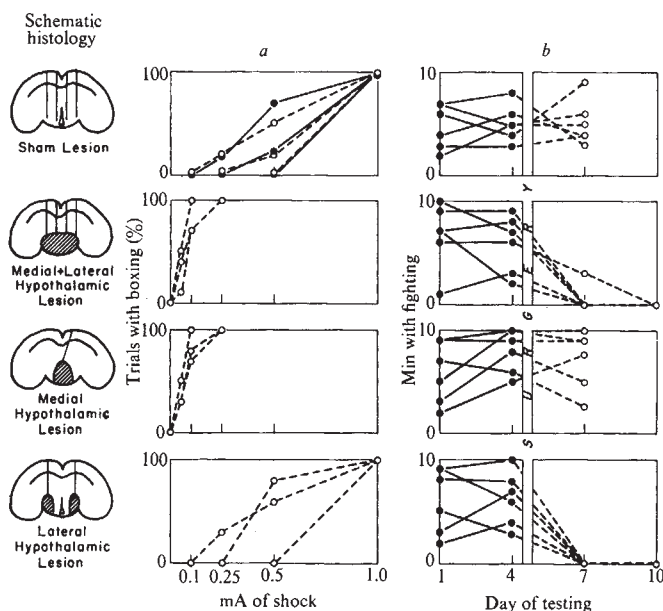


Fig. 1 Effects of hypothalamic lesions in hooded rats on threshold of defence behaviour in the shock box (a) and the persistence of territorial behaviour in home cage (b). Defence behaviour was defined as defensive upright posture and boxing by both members of pairs of lesioned rats. Territorial fighting was defined as the presence of offensive side posture or full attack posture with biting, and it was quantified by the number of minutes during a test session in which one or the other behaviour was exhibited by the rat in his home cage against an intruder. Pre-operative data were not obtained in the shock box because of an interaction between the shock box and territorial testing procedures. One set of data was obtained from normal animals and is shown on the top line, together with post-operative data from sham-lesion rats. ●—●, Pre-operative testing; ○---○, post-operative testing.

Lesions involving both lateral and medial hypothalamus on both sides abolished territorial behaviour and simultaneously enhanced defence behaviour in the shock box, both effects being very strong. Rats which had previously attacked an intruder male within 1 min of the intrusion and persisted with biting and offensive side posture for most of the succeeding 10 min were rendered totally docile in the same situation post-operatively. The intruder might sniff at the rat, wander around him, or even lie down on him, but the rat with the lesion would ignore the intruder or sniff at him and turn away. The same animal, on the other hand, would show defence upright posture and boxing in the shock box at thresholds only one-tenth of the intensity of normal thresholds. Whereas normal rats usually fought only during presentation of the shocks, the rats with lesions usually continued to fight after the shock was discontinued and often fought spontaneously between trials.

By confining lesions to the medial and lateral hypothalamus it was possible to separate the two effects. The enhancement of defence behaviour in the shock box was caused by lesions of the medial hypothalamus; a lesion confined to the lateral hypothalamus on both sides had no effect. The abolition of territorial behaviour was caused by lesions of the lateral hypothalamus; a lesion confined to the medial hypothalamus had no effect.

Table 1 Responses of Observers

Position	Total	Genuine counts		Total	Control counts		P
		Yes	Yes/total		Yes	Yes/total	
Prone (face down)	3,878	558	0.144	9,404	1,050	0.112	<0.001
Supine (face up)	4,682	763	0.163	6,421	887	0.138	<0.001
Side (eye)	3,411	487	0.143	6,448	740	0.115	<0.001
Side (cortex)	3,549	456	0.128	6,256	806	0.129	0.94
Supine (D'Arcy and Porter ¹)	274	65	0.237	1,613	247	0.153	<0.001

It is clear that, for the three cases when the muons passed through the eye, visual effects were observed; these were absent when the particles passed through the cortex. Although the Cherenkov angle in the eye is quite large ($\sim 41^\circ$) and the retina extends over rather more than a hemisphere, it would be expected that the coupling to the retinal receptors of Cherenkov light produced by muons travelling parallel to the visual axis and entering the front of the eye would be more efficient than that for similar particles entering from the rear of the eye. The resultant marked improvement in the detection efficiency for the supine over the prone position does not seem to exist. It has been shown² that it is unlikely that a singly charged fast particle could produce enough visible Cherenkov light to constitute a supra-threshold signal. Our results therefore seem to favour a direct-excitation phenomenon at the retinal level, probably related to that occurring with X-rays³ and with knock-on protons produced by fast neutrons⁴⁻⁶.

W. N. CHARMAN
CHRISTINA M. ROWLANDS

Department of Ophthalmic Optics,
University of Manchester Institute of
Science and Technology

Received May 5, 1971.

¹ D'Arcy, F. J., and Porter, N. A., *Nature*, **196**, 1013 (1962).

² Fazio, G. G., Jelley, J. V., and Charman, W. N., *Nature*, **228**, 260 (1970).

³ Kimeldorf, D. J., and Hunt, E. L., *Ionising Radiation—Neural Function and Behaviour*, 131 (Academic Press, London, 1965).

⁴ Fremlin, J. H., *New Sci.*, **47**, 42 (1970).

⁵ Tobias, C. A., Budinger, T. F., and Lyman, J. T., *University of California Radiation Laboratory Report*, No. UCRL 19868 (1970).

⁶ Charman, W. N., Dennis, J. A., Fazio, G. G., and Jelley, J. V., *Nature*, **230**, 522 (1971).

its metabolites³. As dexbenzetimide is specifically taken up and retained by small nerve endings of the caudate nucleus of the rat³, it is tempting to assume that the binding sites are at or near an acetylcholine receptor.

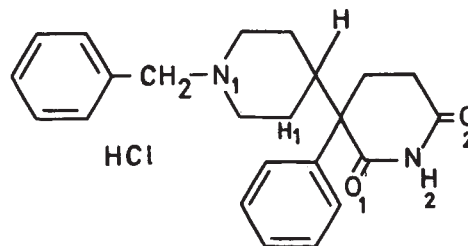


Fig. 1 (±) Benzetimide.

A Stuart-Briegleb model^{4,5} of benzetimide indicates that except at the benzyl moiety, the molecule is rigid with a flat hydrophilic bottom and a lipophilic top. A footprint in plaster-of-paris was made of the hydrophilic side of the benzetimide model showing the imprints of N(1), H(1), O(1), H(2) and O(2). A model of the transconformation of acetylcholine, which is thought to be responsible for the muscarinic activity of the molecule⁶, fits this footprint perfectly. The footprint was tested with a number of S-B models of optically active

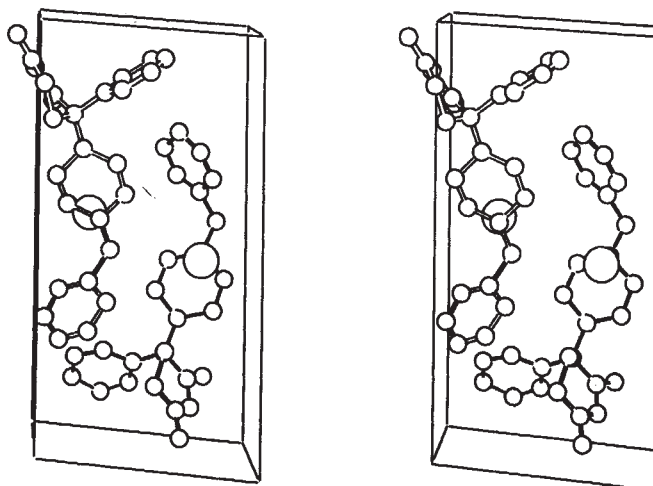


Fig. 2 Stereoscopic plot of the unit cell-content of the dexbenzetimide-HBr crystals. The larger circles represent Br and the small circles represent C, N or O.

The Absolute Configuration and Crystal Structure of the Anticholinergic Drug Dexbenzetimide

THE pharmacological activity of (±) benzetimide (Fig. 1) ((±)-1-benzyl-4-(2,6-dioxo-3-phenyl-3-piperidyl)-piperidine HCl), a potent and persistent anticholinergic agent, acting in both the peripheral and the central nervous system, is due entirely to the (+)-isomer dexbenzetimide¹. The drug is used to abolish Parkinson symptoms sometimes evoked in psychiatric patients being treated with neuroleptic drugs². The anticholinergic properties are due to the unaltered dexbenzetimide and not to

agonists and antagonists with known absolute configuration of the pharmacologically active antipode, but only the models of the active antipode fitted the footprint as the acetylcholine model did. This strongly suggests that the model of benzetimide used in making the footprint is the model of the pharmacologically active antipode, which means that this dextro-rotating antipode must have the S configuration.

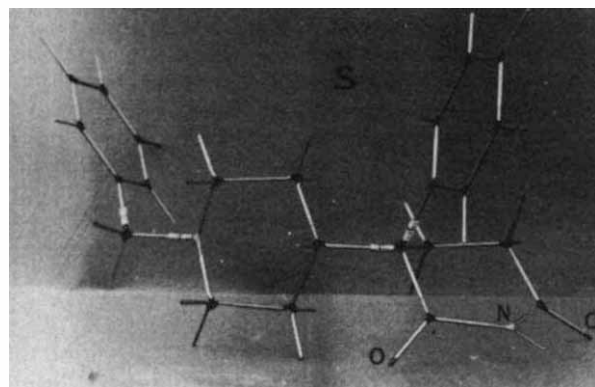


Fig. 3 Dreiding model of dextrobenzetimide of one of the conformations in the unit cell.

On the strength of this we predicted the absolute configuration of the pharmacologically active antipode of 1-trimethylammonium-2-acetoxy cyclopropane^{4,5} which was confirmed by X-ray diffraction⁷. To justify this method we determined the absolute configuration of (+) benzetimide (dextrobenzetimide) by X-ray diffraction. The structure of the triline crystals of dextrobenzetimide-HBr was solved by using a new symbolic phasing procedure, the details of which will be published later (data available on request). The pertinent data are: space group P_1 , cell dimensions $a=7.319$ Å, $b=9.014$ Å, $c=17.49$ Å, $\alpha=94.9^\circ$, $\beta=99.1^\circ$, $\gamma=80.3^\circ$, two formula units in the unit cell, 56 non-hydrogen atoms in the cell. The absolute configuration, S as shown in Fig. 2, was determined by anomalous isotropic refinement of both enantiomorphs, using 2,604 reflexions. It resulted in

$$R_2 \equiv \left(\frac{\sum (F_o - F_c)^2}{\sum F_o^2} \right)^{1/2}$$

values of 18.5% and 18.7% and there is therefore a significant difference between the fit of the observed structure factors and that of the calculated structure factors for each enantiomorph, fixing the absolute configuration to the predicted one, S. A Dreiding model of one of the molecules in the unit cell is shown in Fig. 3.

A. L. SPEK
A. F. PEERDEMAN

Laboratory for Crystal Chemistry,
University of Utrecht,
Catharynesingel 51,
Utrecht

I. VAN WIJNGAARDEN
W. SOUDIJN

Research Laboratories,
Janssen Pharmaceutica,
Beerse

Received March 11, 1971.

- ¹ Janssen, P. A. J., Niemegeers, C. J. E., Schellekens, K. H. L., Demoen, P., Lenaerts, F. M., Van Nueten, J. M., van Wijngaarden, I., and Bruggmans, J., *Arzneimittel-Forsch.* (in the press).
- ² De Smedt, R., Rodrigus, E., Debandt, R., and Bruggmans, J., *J. Clin. Pharmacol.*, **10**, 207 (1970).
- ³ van Wijngaarden, I., *Life Sci.*, **1**, 9, 489 (1970).
- ⁴ van Wijngaarden, I., thesis, Univ. Leyden (1970).
- ⁵ van Wijngaarden, I., Soudijn, W., and Van der Eycken, C., *Life Sci.*, **9**, 1289 (1970).
- ⁶ Archer, S., Lands, A. M., and Lewis, T. R., *J. Med. Pharmacol. Chem.*, **5**, 423 (1962).
- ⁷ Chothia, C., and Pauling, P., *Nature*, **226**, 541 (1970).

Fracture of Bone Materials in Compression at Temperatures between -200°C and $+200^\circ\text{C}$

RECENT studies^{1,2} of bone materials have suggested that the fracture behaviour is sensitively dependent on specimen orientation, microstructure, the presence of external notches, temperature and the deformation rate imposed. The deformation properties of bone have been likened to those expected of composite materials^{2,3}. This report provides further information about the strength of bone and helps to define the criteria which must be satisfied by theoretical models of the mechanical properties.

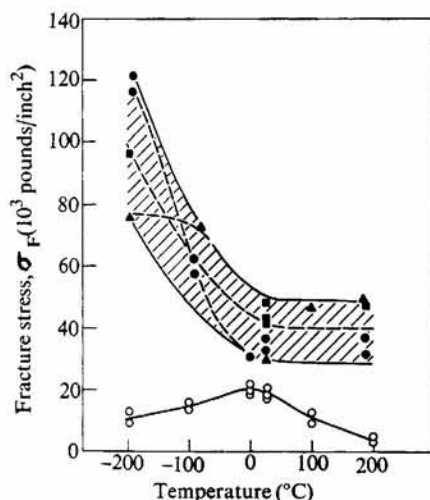


Fig. 1 Compressive and tensile fracture stress of bone at various temperatures. Compression tests: ●, aged, 25°C ; ■, as received; ▲, annealed, 110°C . ○, Tensile results of Bonfield and Li¹.

Specimens for compression tests were made from two different bone materials. Ten cylindrical specimens 0.472 cm in diameter and 1.27 cm in height were made from the section of a steer femur which had been thoroughly dried by ageing for 2 yr in normal atmospheric conditions after the immediate removal of the centre marrow. The specimen axes were essentially parallel to the length of the bone. The specimens showed no macroscopic porosity and were machined on a lathe with a maximum layer removal of 0.025 cm per pass. Another set of ten tetragonal specimens 1.01 cm in height and square cross-section of 0.5 cm per side were produced from wet bovine femur material within two weeks of death. Specimen surfaces were ground flat and parallel to within 0.0025 cm by layer removal per pass equal to or less than 0.025 cm. Five of these specimens were annealed in a vacuum of 10^{-5} mm Hg at 110°C

for 170 h. The specimens were tested within a specially constructed cylindrical compression chamber mounted on a floor model Instron testing machine so that the entire chamber could be immersed in liquid baths at various temperatures⁴. A strain rate of $\sim 10^{-3} \text{ s}^{-1}$ was used.

The fracture stresses required at various test temperatures are shown in Fig. 1 along with the tensile fracture stress results of bovine femur material¹. At room temperature, the measured compressive strengths lie between 29,000 and 48,000 pounds/inch². Within this range, the compressive strength does not change appreciably at temperatures above 0° C, but does increase strongly at temperatures below 0° C. The ratio of the fracture stresses in compression and tension varies from 8.0 to 12.0 at the highest and lowest test temperatures. At room temperature the ratio is between 1.5 and 2.5. The upper limiting values of this ratio may be explained on the basis that a single critical flaw governs the fracture strength according to a Griffith energy release hypothesis⁵. The lower limiting value of this ratio may be associated with brittle fracture behaviour in normally ductile polycrystalline materials whereby the yield stress, as measured in compression, is equated to the brittle (cleavage) fracture stress, as measured in tension⁶.

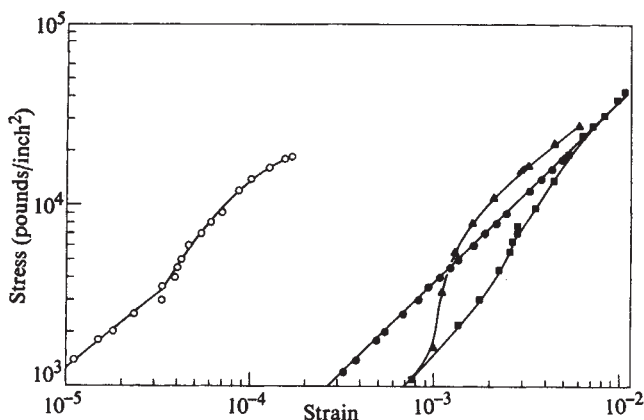


Fig. 2 Stress-strain behaviour of bone in compression or tension at 25° C. ■ and ▲, as in Fig. 1. Tensile results¹: ○, plastic strain only; ●, total strain.

The compressive stress-strain behaviour of two specimens deformed at room temperature is shown in Fig. 2 versus the tensile stress-strain behaviour previously reported on a similar material¹. From the original compression specimen, a linear curve was obtained at large strains that was essentially identical to the extended stress-strain behaviour predicted for the tensile specimen, both specimens giving an elastic modulus of 3.8×10^6 pounds/inch². But this compression specimen showed a yield point drop and an attendant elastic strain decrease at 7,600 pounds/inch². The better fabricated and aligned compression specimen in the annealed condition showed a linear stress-strain behaviour after smaller strains and an increased elastic modulus value of 5.0×10^6 pounds/inch², as expected. This comparison indicates that at room temperature the tensile and compressive stress-strain behaviour of bone material is similar except that fracture occurs in tension at smaller strain values.

The results show that the compressive strength of bone at various temperatures shows a distinctive behaviour which, when compared with tensile results on similar material, produces some new conditions to be explained by any theory proposed to encompass the total deformation and fracture behaviour.

We thank Dr S. B. Mohanty for bone materials and Dr W. L. Phillips for assistance with the measurements. This research has been supported by the Advanced Research Projects Agency

through the Center of Materials Research and by the Office of Naval Research.

R. W. ARMSTRONG
B. ARKAYIN
G. HADDAD

Engineering Materials Group and
Mechanical Engineering Department,
University of Maryland,
College Park, Maryland 20742

Received January 22; revised April 5, 1971.

- ¹ Bonfield, W., and Li, C. H., *J. Appl. Phys.*, **37**, 869 (1966).
- ² Piekarski, K., *J. Appl. Phys.*, **41**, 215 (1970).
- ³ Currey, J. D., *Biorheology*, **2**, 1 (1964).
- ⁴ Wessel, E. T., *Bull. Amer. Soc. Testing Materials*, **211**, 40 (1956).
- ⁵ Orowan, E., *Rep. Prog. Phys.*, **12**, 185 (1948).
- ⁶ Armstrong, R. W., *Phil. Mag.*, **9**, 1063 (1964).
- ⁷ Armstrong, R. W., *Fracture*, 314 (Chapman and Hall, London, 1969).

Synthesis of Cystine in Simulated Primitive Conditions

IN an attempt to utilize the very abundant long wavelength ultraviolet solar radiation for prebiological organic chemistry, a series of experiments was performed in which H₂S was introduced as the long wavelength photon acceptor. These experiments are described in detail elsewhere¹, but in a typical experiment a spherical reaction vessel was filled with methane, ethane, ammonia, water vapour and H₂S and the gases were irradiated in cylindrical geometry with the 2537 Å and/or 1849 Å resonance emission lines of mercury. The gases and their photolysis products were then circulated over a liquid water bath by a greaseless solenoid pump and returned to the reaction vessel (Fig. 1).

In one experiment, the initial mixture contained 612 cm³ of CH₄, 2,024 cm³ of C₂H₆, 1,004 cm³ of NH₃, 542 cm³ of H₂S and 16 cm³ of liquid H₂O. The mixture was irradiated with 2537 Å radiation for 30 h at a gas temperature which ranged from 215° to 360° C. A deep brown viscous liquid was formed and examined by ion exchange chromatography in a Beckman model 120C amino-acid analyser. The identity of the peak which corresponded to cystine was confirmed by adding a known standard chromatographically pure solution of cystine to our brown liquid sample and noting that the appropriate peak increased in amplitude, with no shoulder introduced. The cystine detected was present at a concentration of approximately $5 \times 10^{-3} \mu\text{mol/cm}^3$.

In a second experiment, 591 cm³ of CH₄, 2,010 cm³ of C₂H₆, 1,000 cm³ of NH₃, 549 cm³ of H₂S and 15 cm³ of liquid H₂O were introduced into the reaction vessel and irradiated with 2537 Å and 1849 Å radiation for 2 days, with 2537 Å for 1/2 days and again with 2537 Å and 1849 Å for 9 days. The average gas temperature during this 12 day experiment was 400° C. The deep brown viscous liquid solution produced in this experiment was sequestered for 3 months. When examined with a Beckman model 120C amino-acid analyser, cystine was found but no cysteine; the amount of cystine produced was approximately 0.042 $\mu\text{mol/cm}^3$. The presence of cystine was confirmed by the absence of a shoulder when a cystine standard was performed on a Hitachi model 'KLA-3B' amino-acid analyser (Fig. 2). In this experiment 2 mCi of ¹⁴CH₄ and 1 mCi of ¹⁴CH₃¹²CH₃ were also introduced into the reaction mixture at the beginning of the experiment and the liquid products were examined by two dimensional autoradiographic paper chromatography (Whatman No. 1 paper). The two solvents were 10 methanol : 10 n-butanol : 5 water : 2 ammonia,

and 10 acetone : 10 n-butanol : 5 water : 2 ammonia. The chromatograms were then placed against Kodak medical X-ray film NS-54T and developed by a 1 month exposure. A spot corresponding to cystine was found. The presence of cystine in this experiment can be regarded as confirmation of the results of the previous experiment because cystine has a tendency to oxidize to cysteine.

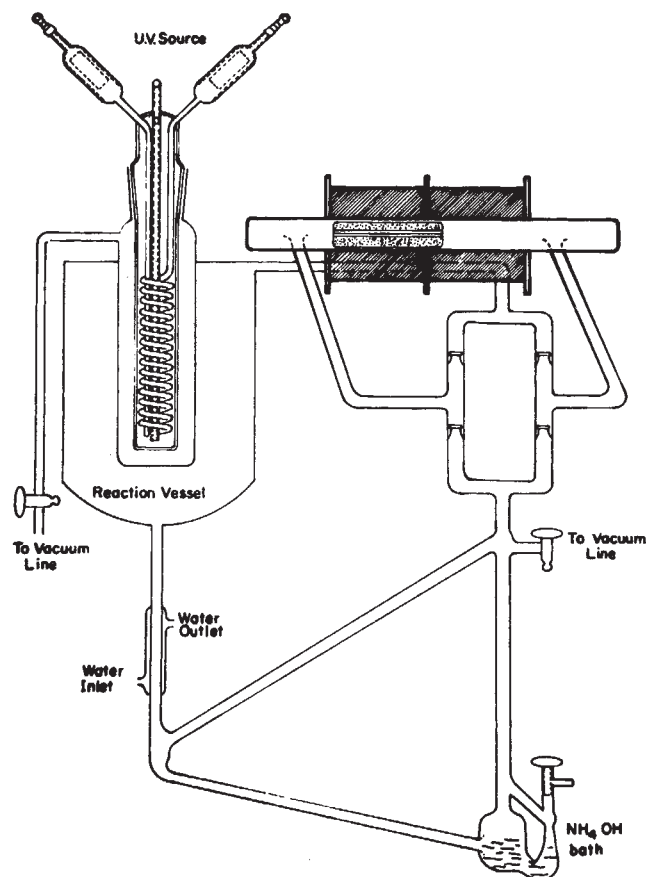


Fig. 1 Schematic diagram of experimental apparatus. Gases irradiated in the reaction vessel are circulated by the Watson pump, upper right, through an ammonia solution (pH 12), lower right.

In a third experiment, 1,638 cm³ of CH₄, 6,055 cm³ of C₂H₆, 3,035 cm³ of NH₃, 1,678 cm³ of H₂S and 50 cm³ of liquid H₂O were introduced into the reaction vessel and irradiated with 2537 Å radiation for 25 days at a temperature of 50° C. Half of the 50 cm³ of coloured liquid product was taken from the aqueous bath, dried under nitrogen and hydrolysed for 22 h with 5.7 M HCl. Although no free cystine was found, a trace was detected with the amino-acid analyser in the acid hydrolysate.

In all three experiments, the closely related α-amino-acid serine was also found. Control experiments—in which the gas was heated to 300–400° C for 11 days but not irradiated, or in which the gas was irradiated at 2537 Å at 20° C for 14 h but in the absence of ethane—gave negative results for amino-acids¹. In all three experiments, we obtained preliminary column chromatographic evidence for the presence of cysteic acid.

In an earlier experiment in which a gaseous mixture of methane, ammonia, water and H₂S was irradiated with 10⁹ rads from an electron beam accelerator, cysteic acid, taurine and cystamine were found². And in another, an aqueous solution of ammonium thiocyanate was irradiated with 2537 Å;

the sulphur-containing amino-acid methionine was identified by autoradiographic paper chromatography with three different solvent systems. In our experiments we found a spot which appeared to have the position and shape of the methionine paper chromatography spot. A known sample of methionine was run on Whatman No. 1 chromatographic paper, eluted and analysed on an AEI model 'MS-902' mass spectrometer. A similar analysis of the unknown spot gave a mass spectrum quite different to that of methionine. Similarly, the addition of a methionine standard to our solution showed the unknown to be the shoulder of the methionine standard (compare Fig. 2).

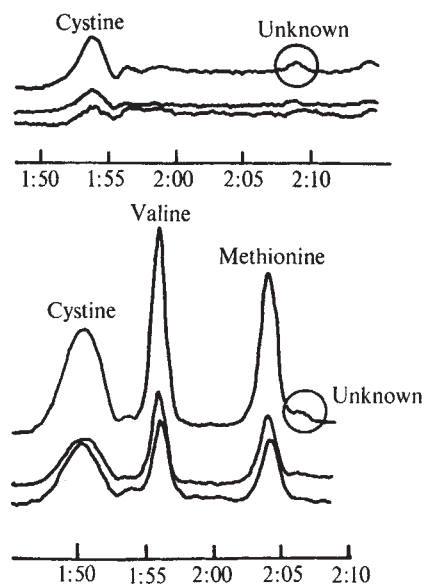


Fig. 2 Ion exchange chromatograms of experimental samples (above) and experimental samples plus chromatographically pure cystine, valine and methionine standards (below) produced by a Hitachi model KLA-3B amino-acid analyser. The coincidence of peaks near elution time 1:50 and the non-coincidence near 2:07 is evidence for the presence of cystine but not of methionine. The elution time phase shift in the two chromatograms, obtained in slightly different conditions, is expected.

The yield of cystine in our experiments was probably considerably larger than we detected. Both cystine and cysteine are known to decompose readily in alkaline solution to pyruvic acid, H₂S, NH₃ and sulphur⁴. Because NH₃ was present in our system, the conditions in aqueous solution were quite alkaline (pH 12). Sulphur polymers up to S₈ were detected by mass spectrometry in the aqueous phase of our system, but these are mostly direct products of H₂S photolysis. The alkaline hydrolysis of cystine regenerates the ammonia and H₂S involved in its photolytic production and leads to a considerable accumulation of pyruvic acid, a substance of particular interest in the context of the Horowitz hypothesis for the reverse evolution of enzymatic reaction chains⁵. Pyruvic acid is the end product of the anaerobic glycolytic pathway ubiquitous in terrestrial organisms. In addition Forbes and Savage^{6,7} have found that visible and long wavelength ultraviolet light incident on alkaline or neutral solutions of cystine in the presence of air leads to a rapid conversion of cystine to alanine-thiosulphonic acid and alanine-thiosulphuric acid, together with smaller amounts of alanine-sulphuric acid, cysteic acid, H₂S and two unidentified amino-acids. Thus, because both alkaline hydrolytic and photolytic destruction of cystine are known to occur in our experimental or post-experimental conditions, these experiments suggest a

plausible mechanism for the high yield production of cysteine and cystine in the early history of the Earth.

This research was supported by the National Aeronautics and Space Administration, the Smithsonian Institution and the US Public Health Service. We thank Nurit Bar-Nun, Robert Goldberg, Jeremy Hribar, Fred McLafferty, James Bartholomew and Arabinda Guha for assistance and advice.

BISHUN N. KHARE
CARL SAGAN

Laboratory for Planetary Studies,
Cornell University,
Ithaca,
New York 14850

Received January 28; revised April 15, 1971.

¹ Sagan, C., and Khare, B. N., *Science*, **173**, 417 (1971).

² Choughuley, A. S. V., and Lemmon, R. M., *Nature*, **210**, 628 (1966).

³ Steinman, G., Smith, A., and Silver, J., *Science*, **159**, 1108 (1968).

⁴ Fruton, J. S., and Simmonds, S., *Biochemistry* (2nd ed.), 58 (Wiley, New York, 1958).

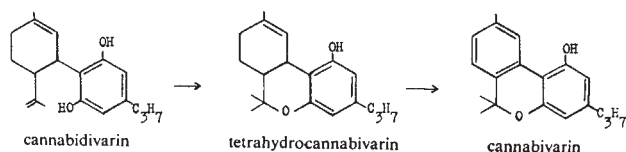
⁵ Horowitz, N. H., *Proc. US Nat. Acad. Sci.*, **31**, 153 (1945).

⁶ Forbes, W. F., and Savage, W. E., *Photochem. Photobiol.*, **1**, 1 (1962).

⁷ Forbes, W. F., and Savage, W. E., *Photochem. Photobiol.*, **1**, 77 (1962).

Cannabivarin and Tetrahydrocannabivarin, Two New Constituents of Hashish

We have identified two more constituents of hashish to add to the constituents of hashish already known¹. In 1969 Vollner *et al.*² identified cannabidiol, a cannabidiol homologue in which the side chain is C₃H₇ instead of C₅H₁₁. All cannabinoids found until then had contained an olivetyl group (n-amyresorcinol). This was the first cannabinoid found which contained a divarinyll group (n-propylresorcinol). Because many constituents are derived from cannabidiol and cannabidiolic acid, Vollner *et al.* predicted that hashish would yield more constituents derived from cannabidiol, and indeed Gill *et al.*³ found in 'Tincture of Cannabis' (BPC) a Δ¹-tetrahydrocannabinol homologue with C₃H₇, instead of C₅H₁₁ as the side chain.



In all the Nepal samples we studied cannabidiol, tetrahydrocannabinol and cannabinol were also present, and so it seems that two parallel biosynthetic processes are possible in the same cannabis product: cannabidiol (CBD)→tetrahydrocannabinol (THC)→cannabinol (CBN) and cannabidiol (CBD)→cannabidiol (CBDV)→tetrahydrocannabivarin (THCBV)→cannabivarin (CBV) (Fig. 1).

The sequence of the R_F values of the different constituents can be explained as follows (Fig. 2). The hydrogen bond between the stationary phase dimethylformamide and the phenolic group of the three cannabinoids, containing the propyl group, is stronger than the bond between dimethylformamide and the cannabinoids containing the amyl group. Supposing an equal solubility in the solvent cyclohexane, the R_F values of the three cannabinoids with the propyl group are lower than the R_F values of the corresponding cannabinoids with the amyl group. Indeed the following sequence of R_F values is obtained: cannabidiol < cannabidiol, cannabivarin < cannabinol and tetrahydrocannabivarin < tetrahydrocannabinol. The quantitative determination was carried out by gas liquid chromatography on a 'SE 52' column (Fig. 3).

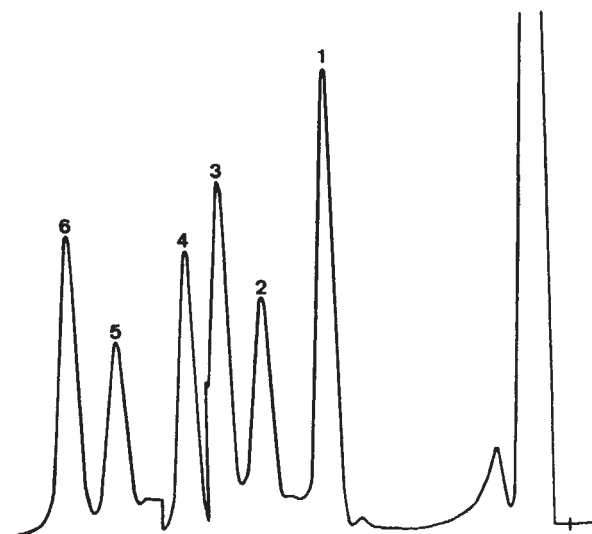


Fig. 3 Gas liquid chromatography of a sample of Nepal hashish. The sample was extracted with petroleum ether and after evaporation of the petroleum ether the residue was dissolved in chloroform. The separation was carried out on a column of 'SE 52' (5% on 'Gas Chrom Q'), column temperature 225°–280° C, 6°/min, N_2 flow 40 ml./min, flame ionization detector. Peak numbering: cannabidiol (1), tetrahydrocannabivarin (2), cannabivarin (3), cannabidiol (4), tetrahydrocannabinol (5), cannabinol (6).

The retention times of the chief constituents of the samples of Nepal hashish were on the 'SE 52' column (column temperature 225°–280° C, 6°/min, N_2 flow 40 ml./min): cannabidiol 4 min 19 s, tetrahydrocannabivarin 5 min 29 s, cannabivarin 6 min 12 s, cannabidiol 6 min 48 s, tetrahydrocannabinol 8 min 00 s, and cannabinol 8 min 53 s. The peak areas were measured by height × width at half height. Table 1 summarizes the quantitative determination of three samples of Nepal hashish. The three cannabinoids containing the divariny group seem to be present in large quantities in proportion to the other well known cannabinoids. The maximum percentages of the total amount of the six chief constituents we found were 15.8% for cannabivarin, 5.7% for tetrahydrocannabivarin and 12.3% for cannabidiol. These findings are significant not only for chemistry but also in assessing the biological activity of samples of hashish containing these constituents.

Tetrahydrocannabivarin will undoubtedly have psychotomimetic properties and is a more polar compound than tetra-

Table 1 Amounts of Single Components in Nepal Hashish as Percentage of Total Cannabinoids: Cannabinol, Tetrahydrocannabinol, Cannabidiol, Cannabivarin, Tetrahydrocannabivarin and Cannabidiol

	Sample A	Sample B	Sample C
Cannabinol	22.1	24.8	30.3
Tetrahydrocannabinol	11.5	3.4	5.5
Cannabidiol	35.9	41.1	41.2
Cannabivarin	12.5	15.8	11.6
Tetrahydrocannabivarin	5.7	3.0	2.3
Cannabidiol	12.3	11.9	9.1

The quantitative determination was carried out by measuring the peak areas on a gas chromatogram, made on an 'SE 52' column.

hydrocannabinol. Its biological activity will be smaller, since from earlier studies¹⁵ with synhexyl (a THC-like compound), in which the side chain was varied, it seemed that the activity in the n-alkyl series rises to a maximum at n-hexyl and then falls off again. But we think the more polar character of tetrahydrocannabivarin may influence the resorption, the onset of action, the formation of polar metabolites and the excretion in man.

In relation to this, two recent studies are of interest. Gill *et al.*³ found that tetrahydrocannabivarin is 4.8 times less active than tetrahydrocannabinol in producing a cataleptic effect in mice. Tetrahydrocannabivarin, however, contributes significantly to the early part of the response of mice to crude cannabis, while tetrahydrocannabinol itself acts very slowly. Second, from the investigations of Lemberger, Silberstein, Axelrod and Kopin¹⁶ it can be concluded that tetrahydrocannabinol persists for many days in normal volunteers and that it is metabolized in man and excreted as polar metabolites in urine and faeces. These observations enable us to conclude that the presence of tetrahydrocannabivarin in a sample of hashish will contribute significantly to the psychotomimetic activity of that sample.

It is also likely that tetrahydrocannabivarin will have an additive or a synergistic effect to the tetrahydrocannabinol effect. We have found that in many samples of hashish a considerable quantity of cannabidiol, tetrahydrocannabivarin and cannabivarin is present. The identification and the quantitative determination contribute to a more exact chemical knowledge of the constituents and their biosynthesis and allow a better understanding of the different biological activities of hashish samples.

FRANS W. H. M. MERKUS

RC Hospital,
Sittard,
The Netherlands

Received April 18, 1971.

- ¹ Mechoulam, R., *Science*, **168**, 1159 (1970).
- ² Vollner, L., Bieniek, D., and Korte, F., *Tetrahedron Lett.*, 145 (1969).
- ³ Gill, E. W., Paton, W. D. M., and Pertwee, R. G., *Nature*, **228**, 134 (1970).
- ⁴ Merkus, F. W. H. M., *Pharm. Weekblad*, **106**, 49 (1971).
- ⁵ Merkus, F. W. H. M., *Symposium 6, Chromatography and Electrophoresis*, Brussels (in the press).
- ⁶ Aramaki, H., Tomiyasu, N., Yoshimura, H., and Tsukamoto, H., *Chem. Pharm. Bull.*, **16**, 822 (1968).
- ⁷ Karlsen, J., Exler, Th. J. H., and Baerheim Svendsen, A., *Pharm. Weekblad*, **104**, 583 (1969).
- ⁸ Machata, G., *Arch. Toxikol.*, **25**, 19 (1969).
- ⁹ de Faubert Maunder, M. J., *J. Pharm. Pharmacol.*, **21**, 334 (1969).
- ¹⁰ Parker, K. D., Wright, J. A., Halpern, A. F., and Hine, C. H., *Bull. Narcotics*, **20** (No. 4), 9 (1968).
- ¹¹ Mechoulam, R., and Gaoni, Y., *Tetrahedron*, **21**, 1223 (1965).
- ¹² Korte, F., and Sieper, H., *J. Chromatog.*, **13**, 90 (1964).
- ¹³ Budzikiewicz, H., Alpin, R. T., Lightner, D. A., Djerassi, C., Mechoulam, R., and Gaoni, Y., *Tetrahedron*, **21**, 1881 (1965).
- ¹⁴ Merkus, F. W. H. M., *Pharm. Weekblad*, **106**, 69 (1971).
- ¹⁵ Todd, A. R., *Experientia*, **2**, 55 (1946).
- ¹⁶ Lemberger, L., Silberstein, S. D., Axelrod, J., and Kopin, I. J., *Science*, **170**, 1320 (1970).

Acid Monoamine Metabolites in Cerebrospinal Fluid during Methadone Maintenance

SOME studies of the interaction of narcotic analgesics and brain monoamine systems have implicated brain monoamines in acute and long term effects of the principal narcotics¹, but interspecies variation makes it difficult to apply these results to man. Techniques are now available which use monoamine metabolites in cerebrospinal fluid (CSF) as indicators of central monoamine metabolism²⁻⁴. Using measures which reflect central 5-hydroxytryptamine (serotonin) and dopamine synthesis, we studied patients on methadone maintenance therapy for heroin addiction.

Twenty-five determinations were made in sixteen male (ages 25-46) and five female (ages 25-32) heroin addicts who were taking single daily doses of methadone (25-135 mg/day). For ten determinations, 4 ml. CSF was obtained by lumbar tap while a group of subjects was taking methadone only. Before fifteen further determinations, another group of subjects were given probenecid, 3.0 g/day orally for 2.5 days before CSF sampling as described before^{5,6}. Probenecid blocks the egress of acid monoamine metabolites from CSF and brain and as a result metabolite concentrations increase⁷⁻⁹. Acid monoamine metabolite values in CSF obtained after the use of probenecid may therefore reflect more closely than baseline values the formation rates of the metabolites within the central nervous system. Samples were assayed fluorimetrically for 5-hydroxyindoleacetic acid (5HIAA, acidic metabolite of serotonin) and homovanillic acid (HVA, acidic metabolite of dopamine)²⁻⁴. Similar non-paired samples with and without probenecid were obtained from a group of psychiatric in-patients (within 10 days of hospital admission, no drugs for at least a week) and from a group of paid inmate volunteers. All subjects gave informed consent. Methadone added to CSF caused no quenching or other interference with acid monoamine metabolite readings except at very high concentrations (1 mg methadone/ml. CSF). In studies involving mice, methadone in substantially larger doses did not interfere with the ability of probenecid to block the egress of acid monoamine metabolites from brain¹⁰.

Unpaired comparisons for 5HIAA and HVA were made between subjects in each category (addicts, psychiatric patients, and inmates) who took probenecid and those who did not. Intergroup comparisons were made for the probenecid and non-probenecid conditions. Addicts in the probenecid condition taking less than 90 mg methadone/day were compared with those taking 90 mg/day or more. Mean values for 5HIAA and HVA were compared by a *t* test (two tailed).

Without probenecid, compared with inmates, 5HIAA values were significantly lower in the psychiatric and addict groups ($P < 0.001$, Table 1). Within the groups, subjects taking probenecid, compared with those not taking probenecid, had higher values for CSF 5HIAA in the case of inmates ($P < 0.005$) and psychiatric patients ($P < 0.001$), but not in the addict group. On probenecid, the addicts (mean methadone dose 87.4 mg/day) showed a significantly lower value for CSF 5HIAA than inmates ($P < 0.001$) and psychiatric patients ($P < 0.005$). Without probenecid, the three groups' means did not differ in HVA. Within each group, subjects on probenecid had a higher CSF HVA value than those without probenecid. But the addict group on probenecid showed the lowest HVA value, significantly lower than the psychiatric group ($P < 0.01$) but not the inmate group. Addicts taking less than 90 mg of methadone/day as a group had a significantly higher mean value for CSF 5HIAA than those taking 90 mg or more/day. The means ($\pm$ s.e.) were 40.8 ± 7.3 ng/ml. and 23.8 ± 3.2 ng/ml. respectively ($P < 0.05$). Although not significant, the same trend was found for CSF HVA values where the corresponding means were 77.9 ± 10.4 ng/ml. (actual mean methadone dose 66 mg/day) and 52.4 ± 16.2 ng/ml. (actual mean methadone

dose 107 mg/day). A daily 90 mg dose is approximately the average maintenance dose in our subjects. Taken altogether, these data indicate that methadone suppressed the formation of 5HIAA and possibly HVA in the central nervous system of the addicts. These results do not differentiate definitely the possible effects on CSF 5HIAA and HVA of addiction to heroin compared with methadone maintenance. But, whatever the effect of heroin addiction, we can say that full maintenance doses of methadone resulted in a greater decrease in CSF 5HIAA and HVA than lower doses. The mechanism underlying this effect cannot be specified at this point, for methadone may be affecting processes of synthesis (including availability of amine precursors) or storage and release in our subjects. Although not the focus of this report, the finding of a decrease in CSF 5HIAA in a psychiatric population is consistent with previous studies¹¹⁻¹³. The mechanism of this finding is under investigation.

Table 1 Concentrations of 5HIAA and HVA in the Lumbar CSF of Human Subjects with and without Probenecid Pretreatment

Group	5HIAA		HVA	
	Without probenecid	With probenecid	Without probenecid	With probenecid
I	23.2 ± 2.9 (10)	32.0 ± 4.2 (15)	25.3 ± 7.5 (10)	64.3 ± 10.1 (15)
II	29.6 ± 2.5 (36)	49.9 ± 4.1 (15)	26.0 ± 4.2 (34)	111.5 ± 13.3 (15)
III	43.5 ± 1.7 (18)	59.4 ± 4.6 (20)	23.2 ± 5.9 (17)	86.1 ± 8.2 (16)

Group I are addicts on methadone, group II are psychiatric patients, group III are inmates. Values are ng of the free acid/ml. CSF $\pm$ s.e. with numbers of determinations in parentheses. Mean dose of methadone for addicts with and without probenecid was 87.4 and 65.5 mg per day respectively. Mean doses are not significantly different ($P = 0.2$).

A number of studies in animals suggest that functional monoamine systems are necessary for both the acute and long term effects of the narcotic analgesics. In the rat, lesions of the midbrain raphe (which destroy the main serotonin neurone group) increased sensitivity to shock and decreased the analgesic effect of morphine^{14,15}. Further, reserpine and tetra-benazine antagonized analgesia and tolerance in mice^{16,17}. These effects were reversed by 5-hydroxytryptophan and L-dihydroxyphenylalanine, precursors of serotonin and dopamine respectively¹⁴⁻¹⁹. Monoamine oxidase inhibitors increase the toxicity of narcotic analgesics, probably by increasing levels of serotonin¹⁹. Further, inhibitors of serotonin and catecholamine synthesis have been reported to increase sensitivity to pain and to antagonize acute and long term narcotic effect²⁰⁻²². These studies, which employ techniques that disrupt monoamine systems, do not explain the effect of narcotics on monoamine turnover, but they suggest that monoamines are utilized in the production of acute and long term narcotic effects. Earlier studies of the effects of narcotics on brain levels of serotonin and noradrenaline showed minimal changes¹. Some investigators have utilized measurements of monoamine synthesis and turnover. Way and Haubrich found evidence of increased synthesis of serotonin after morphine had been given to mice and rats²³⁻²⁵. Others have been unable to reproduce these results^{26,27}. We have shown that acute and chronic doses of methadone increased brain 5HIAA in mice¹⁰. In studies utilizing radioactive tyrosine, Clouet and Ratner reported increased incorporation of radioactivity into both dopamine and noradrenaline after acute and long term treatment of rats with morphine²⁸. The results reported here are in contrast with most of the animal data²³⁻²⁷. As measured by the formation of

acidic monoamine metabolites in CSF, serotonin and probably dopamine synthesis were decreased, at maintenance levels of methadone in our patients. Whether these results reflect a different effect of methadone or narcotics in general on monoamine systems in man compared with other species is still unclear.

While this paper was being reviewed, Tamarkin, Goodwin and Axelrod reported similar findings in three addicts on methadone²⁹.

This work was supported by a US Public Health Service grant (M. B. B., jun.). Amanda Smith and Angelica Rozitis gave technical assistance.

MALCOLM B. BOWERS, JUN.
HERBERT D. KLEBER
LINDA DAVIS

Yale University Department of Psychiatry,
and Drug Dependence Unit,
Connecticut Mental Health Center,
New Haven,
Connecticut

Received January 11; revised April 23, 1971.

- ¹ Harris, L. S., *Fed. Proc.*, **29**, 28 (1970).
- ² Anden, N. E., Roos, B. E., and Werdinius, B., *Life Sci.*, **2**, 448 (1963).
- ³ Ashcroft, G. W., and Sharman, D. F., *Brit. J. Pharmacol. Chemother.*, **19**, 153 (1962).
- ⁴ Gerbode, F., and Bowers, jun., M. B., *J. Neurochem.*, **15**, 1053 (1968).
- ⁵ Olsson, R., and Roos, B. E., *Nature*, **219**, 502 (1968).
- ⁶ Bowers, jun., M. B., *Brain Res.*, **15**, 522 (1969).
- ⁷ Guldberg, H. C., Ashcroft, G. W., and Crawford, T. B. B., *Life Sci.*, **5**, 1571 (1966).
- ⁸ Bowers, jun., M. B., and Gerbode, F., *Life Sci.*, **7**, 773 (1968).
- ⁹ Bowers, jun., M. B., *Life Sci.*, **9**, 691 (1970).
- ¹⁰ Bowers, jun., M. B., and Kleber, H. D., *Nature*, **229**, 134 (1971).
- ¹¹ Ashcroft, G. W., Crawford, T. B. B., Eccleston, D., Sharman, D. F., MacDougall, E. J., Stanton, J. B., and Binns, J. K., *Lancet*, ii, 1049 (1966).
- ¹² Dencker, S. J., Malm, U., Roos, B. E., and Werdinius, B., *J. Neurochem.*, **13**, 1545 (1966).
- ¹³ Bowers, jun., M. B., Heninger, G. R., and Gerbode, F., *Intern. J. Neuropharmacol.*, **8**, 255 (1969).
- ¹⁴ Lints, C. E., and Harvey, J. A., *J. Comp. Physiol. Psychol.*, **67**, 23 (1969).
- ¹⁵ Saminin, R., Gumulka, W., and Valzelli, L., *Europ. J. Pharmacol.*, **10**, 339 (1970).
- ¹⁶ Rudzik, A. D., and Mennear, J. H., *J. Pharm. Pharmacol.*, **17**, 326 (1965).
- ¹⁷ Takagi, H., and Kuriki, H., *Intern. J. Neuropharmacol.*, **8**, 195 (1969).
- ¹⁸ Lints, C. E., and Harvey, J. A., *Physiol. Beh.*, **4**, 29 (1969).
- ¹⁹ Rogers, K. J., and Thornton, J. A., *Brit. J. Pharmacol.*, **36**, 460 (1969).
- ²⁰ Tenen, S. S., *Psychopharmacologia*, **10**, 204 (1967).
- ²¹ Tenen, S. S., *Psychopharmacologia*, **12**, 278 (1968).
- ²² Eidelberg, E., and Schwartz, A. S., *Nature*, **225**, 1152 (1970).
- ²³ Way, E. L., Loh, H. H., and Shen, F., *Science*, **162**, 1290 (1968).
- ²⁴ Loh, H. H., Shen, F., and Way, E. L., *Biochem. Pharmacol.*, **18**, 2711 (1969).
- ²⁵ Haubrich, D. R., and Blake, D. E., *Fed. Proc.*, **793** (1969).
- ²⁶ Marshall, I., and Grahame-Smith, D. G., *Nature*, **228**, 1206 (1970).
- ²⁷ Cheney, D. L., Goldstein, A., Algeri, S., and Costa, E., *Science*, **171**, 1169 (1971).
- ²⁸ Clouet, D. H., and Ratner, M., *Science*, **168**, 854 (1970).
- ²⁹ Tamarkin, N. R., Goodwin, F. K., and Axelrod, J., *Life Sci.*, **9**, 1397 (1970).

Life Cycle of *Tripedalia cystophora* Conant (Cubomedusae)

THE Cubomedusae, commonly called "box jellies" or "sea wasps" because of their shape and, for some, their severe sting, are inhabitants of neritic tropical regions of the oceans. Though they have been known for more than 200 yr and the morphology of several species has been investigated¹, little is known of their

life histories. Conant¹, in Jamaica, was able to rear the planula of *Tripedalia cystophora* to a four-tentacled polyp. Okada², in Japan, reared *Carybdea rastoni* to approximately the same stage. In neither case did the polyps live to an age which revealed their unusual nature. The opinion, held by many zoologists, that the Cubomedusae are an aberrant order of the Class Scyphozoa has therefore derived from a knowledge of the medusa generation alone. This belief, and the view of some authors³⁻⁶ that the polyp is the stem form of all recent Cnidaria, have led to efforts to elucidate the life cycle of a member of this order.

Unlike other Cubomedusae, the fertilized eggs of *Tripedalia* develop into planulae in the gastric pockets of the female medusa. When the planulae are mature, they are released within 2 days. They are then slightly pyriform, have a diameter of 0.13 mm, and contain a yellow-brown pigment. The planulae settle within 2 days. They have a preference for bivalve shells and darkness but will settle on glass or plastic. Two to three days after settlement a polyp with a mouth and four tentacles is formed. Although naked at first, the polyp's base is enveloped by a thin transparent periderm when the four-tentacle stage is achieved. When the polyps begin to feed they grow rapidly.

When 0.5 mm long, with five or six tentacles, the polyps begin to produce asexual buds from the basal body wall. The buds resemble those of *Hydra* and acquire a functional mouth and tentacles before they are released. On detachment, the two to four-tentacled bud or secondary polyp elongates and one of its tentacles becomes much longer than the others. It is capable of gliding, crown first, over the substrate by use of this elongated tentacle. This secondary polyp soon attaches, becomes pyriform, develops a peridermal sheath about the base, and buds off more polyps in the same manner as the primary polyp. At an age of 8-10 weeks the polyps, either primary or secondary, have a single whorl of seven to nine tentacles, a body length of 0.8-1.0 mm, and appear to be fully grown (Fig. 1).

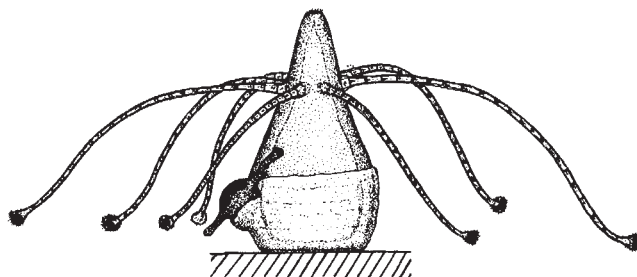


Fig. 1 *Tripedalia cystophora*. Adult polyp; basally, on the left, is a young secondary polyp just before detaching. Length = height of the body is 1.0 mm (drawn by F. Heckmann).

The chief features of the solitary polyp are its long, contractile, cone-shaped peristome and solid, completely retractile, capitate tentacles which bear nematocysts only at their tips. Scyphopolyp features such as a cruciform-shaped mouth, peristomial pits, gastric septa and pockets, septal funnels and muscles, and thick mesogloea are lacking. Only at the time of transformation to a medusa does a tetra-radial symmetry appear. The *Tripedalia* polyp thus more closely resembles a hydropolyp than a scyphopolyp.

The polyp of *Tripedalia* is also unique in that it undergoes metamorphosis into a single medusa. The first evidence of medusa formation is the transformation of the polyp crown to a quadrangular shape. The polyp tentacles then, in no particular order, congregate at the four corners (Fig. 2A). The bases of the tentacles, or coalesced bases of several tentacles, thicken and develop small pigment spots (Fig. 2B). At the same time, the distal parts of the tentacles are resorbed. Ultimately polyp

tentacles, either singly or as a fused group, become the four rhopaloids. Before the polyp tentacles are resorbed, the four primary medusa tentacles appear, *de novo*, between the four rhopaloids. These are hollow, very long, pointed, and are fringed with annular nematocyst batteries. The histology of the developing medusa will be described in a later report, but it can be stated here that the substance of the polyp is completely converted into the tissues of the medusa. At water temperatures of 28°–29° C, metamorphosis to a medusa is completed in 4–5 days. Growth time from planula or newly liberated bud to onset of metamorphosis is 10–12 weeks.

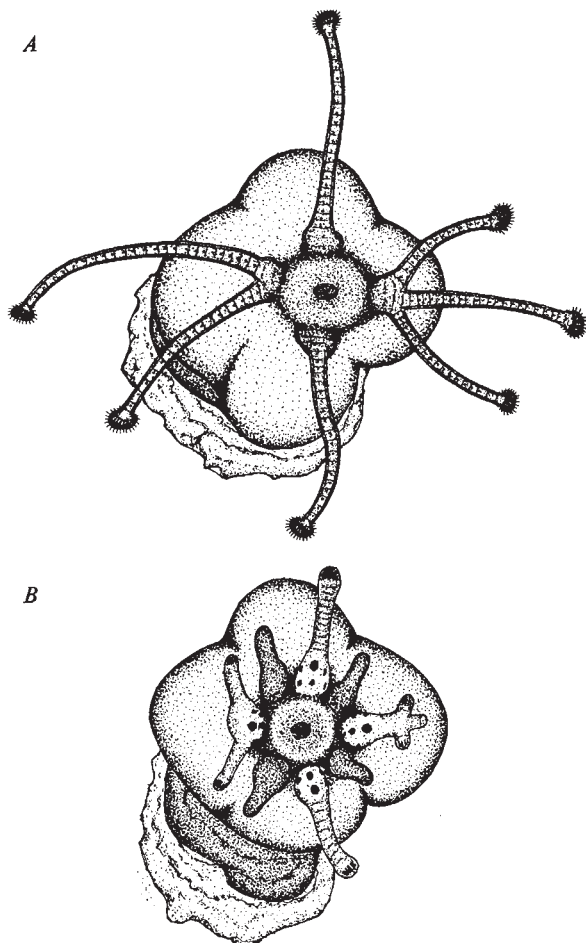


Fig. 2 *Tripedalia cystophora*. A, Adult polyp in the tetra-rotate stage of the beginning of metamorphosis into the medusa; B, Same polyp 2 days later (drawn by F. Heckmann).

As the medusa begins to pulsate, it detaches from within the peridermal cup and swims away in the characteristic manner of a Cubomedusa. The newly liberated medusa (Fig. 3) has a bell diameter of 1.0–1.3 mm and four primary tentacles that lack pedalia. A day later a new small tentacle appears on either side of each of the four primary ones, bringing the tentacles to full complement. Later, the proximal part of each tentacle flattens to become the pedaliolum. In 10–12 weeks the medusa attains full size and sexual maturity.

Several features of the cubopolyp distinguish it from both a hydropolyp and a scyphopolyp. The more salient of these are the total conversion of the polyp into a medusa, a radial symmetry, and the absence of most of the typical scyphopolyp features. These, together with the morphological peculiarities of the medusa generation, suggest that the Cubomedusae may

not be Scyphozoa at all. They possibly may represent an evolutionary link between the Scyphozoa and Hydrozoa and conceivably could be considered to comprise a taxon of comparable rank.

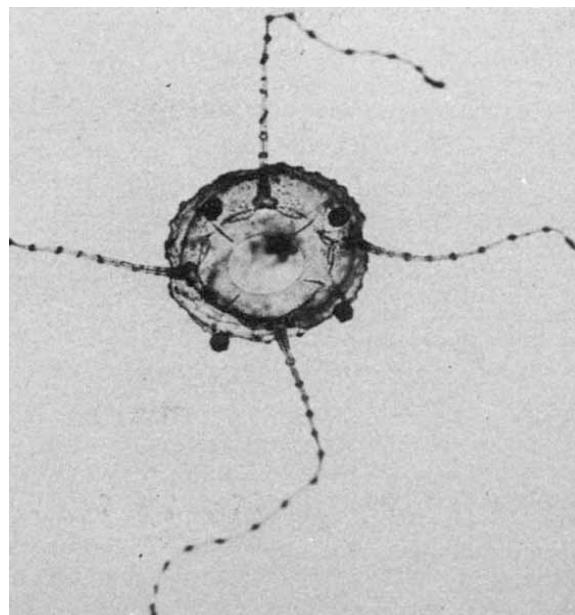


Fig. 3 *Tripedalia cystophora*. Young medusa just after metamorphosis from polyp, reared in laboratory; bell margin above; diameter of the bell is 1.3 mm (photograph by B. Werner).

This study was conducted at the Biologische Anstalt Helgoland and the Department of Marine Sciences, University of Puerto Rico, Mayagüez. It was supported by a grant from the US Department of the Interior, Fish and Wildlife Service, Bureau of Commercial Fisheries, with matching funds from the University of Puerto Rico and was coordinated by the Fisheries Development Program, Department of Agriculture, Commonwealth of Puerto Rico. We thank Sir Frederick S. Russell for reading the manuscript.

BERNHARD WERNER

Biologische Anstalt Helgoland,
2 Hamburg 50,
Palmaille 9

CHARLES E. CUTRESS
JOHN P. STUDEBAKER

Department of Marine Sciences,
University of Puerto Rico,
Mayagüez

Received April 27, 1971.

- ¹ Conant, F. S., *Mem. Biol. Lab. Johns Hopkins Univ.*, 4, 1 (1898).
- ² Okada, Y. K., *Bull. Biol. France Belg.*, 61, 241 (1927).
- ³ Chapman, D. M., in *Symp. Zool. Soc. London* (edit. by Rees, W. R.), 16 (Academic Press, London, 1966).
- ⁴ Thiel, H., in *Symp. Zool. Soc. London* (edit. by Rees, W. R.), 16 (Academic Press, London, 1966).
- ⁵ Uchida, T., *Bull. Mar. Biol. Stat. Asamushi, Tôhoku Univ.*, 13, 247 (1969).
- ⁶ Werner, B., *Zool. Anz. Suppl.*, 33, 159 (1970).

BOOK REVIEWS

Science and Society

Science, Man and Society. By Robert B. Fischer. Pp. viii+124. (Saunders: Philadelphia, London and Toronto, March 1971.) £1.25.

The Scientist's Role in Society: a Comparative Study. By Joseph Ben-David. Pp. xi+207. (Prentice-Hall: Englewood Cliffs, New Jersey, June 1971.) \$6.95 cloth; \$2.95 paper.

DR FISCHER observes that traditional science courses are organized around particular parts of the subject matter of science. They do not give insight into the relevancy of science to man and to society, when people have to face serious social and political issues in which science is a major factor.

Various approaches are being tried to remedy this situation. One is for the science faculties to turn the problem over to the faculties of philosophy and history. Dr Fischer dismisses this as "passing the buck", as it usually turns out to be no solution. Courses in science may be replaced with courses about science. He thinks this is liable to leave the student with no clear grasp of any important principle. Nor is he in favour of organizing science teaching around topical themes such as pollution: these are subject to fashion. His book contains the selection which he considers suitable.

He stresses that science is a dynamic, human activity, limited to things accessible to the senses. He warns against non-dynamic words such as "systematic" and "organized". The understanding of concepts is gained from experience, and, as Einstein says, "the whole of science is nothing more than a refinement of everyday thinking".

Dr Fischer quotes briefly sketches of Priestley, Cavendish and Faraday as contrasting scientific types. Then he compares the scientists of today with those of two centuries ago. They have more to learn, and even then are deeply acquainted with only a limited field. The long training uniformizes their knowledge and habits, to fit them for niches in the vast modern scientific activity.

He relates the present crisis in universities to the growth of science. The universities have become a complex of competing subjects and factions, described by Clark Kerr as the "multiversity", in contrast to the ancient "university". Some of the courses, intended to deepen students' general understanding of science, have increased their alienation. The more they know about

science, the less they like it. Man has got to the Moon, but not solved the problems of poverty and crime.

It is essential to emphasize that science is subject to man, who is a thinking, feeling, doing being. It is up to man to decide whether science shall be allowed to have dehumanizing effects.

Dr Fischer has written a wise and useful little book which should be helpful to many students, and their teachers.

What help is provided by Dr Ben-David's sociological monograph? He discusses the development of science especially in Britain, France, Germany and the United States. He says that "social conditions do not generate intellectual ability and moral responsibility, they only provide the conditions for their exercise". Accordingly, he interprets the foundation of modern science in seventeenth century Britain as due to people who found empirical natural science "a cognitive structure consistent with their interests in a changing, pluralistic and future-oriented society". The conceptual development of empirical natural science was, he says, quite independent of social circumstances.

In the society of twentieth century United States, the "enterprising system of universities working within a pluralistic, educational, and economic system has created an unprecedentedly widespread demand for knowledge and research and has turned science into an important economic resource". This system has encouraged scientific creativity for its own sake by creating a very wide foundation for pure research. However, the system is in a state of delicate balance between scientific and scholarly creativity and the demands of the economic and political powers. This balance is more delicate than elsewhere because "the pluralistic entrepreneurial structure and expansive system of science and higher education require a much greater involvement of the universities in the affairs of society. This is the price paid for the greater support of science and scholarship". A large section of American youth now receives university education in science. Consequently, "in spite of the greater decentralization of political and economic life", US universities have become "one of the most suitable centres of political activism".

Dr Ben-David believes that there was a comparative decline in British science in the second half of the eighteenth century. It is true that Newtonian science declined, but he does not see that that

was already no longer in the first line. The industrial revolution posed new problems, symbolized by the steam engine and the concept of energy, which led to modern physics. Science in Britain changed its direction, founding the line of the future. In France Lagrange and Laplace carried Newtonian science to its apogee, but they were completing old science rather than founding new. If the theory of gravitation is the scientific apotheosis of the British mercantile civilization, the theory of energy is that of the industrial revolution. Ben-David does not perceive in these major social movements examples of the prime forces which have created science.

He comments on the intellectual freedom in German universities in the nineteenth century, while they were the media for nationalistic and anti-semitic propaganda. He says: "it is difficult to determine with any certainty the reason that so many of the 'liberal' elements accepted this situation". Then, he remarks that in the early 1930s "the visiting scientists saw the German university in the light of its ideal self: as a seat of the purest learning for its own sake and an unequalled centre of overall excellence".

In fact, as a visitor to Germany at that period, I was painfully struck by the gap between the high Berlin scientific life and the brutalities done to and by the rank-and-file population. The reason why German scientists put up such a poor show against both German imperialism in the nineteenth century and Nazism in the twentieth was that they had a false philosophy. They believed that "science" was a thing in itself, an affair of the "scientific community", an exalted intellectual endeavour, above the vulgarity of common affairs. Dr Ben-David's book illustrates why "passing the buck" to the sociologists also provides no solution of the problem of science, man and society.

J. G. CROWTHER

Objective Sense

Rationality. Edited by Bryan R. Wilson. (Key Concepts in the Social Sciences.) Pp. xviii+275. (Blackwell: Oxford, November 1970.) £2.75.

ALTHOUGH this collection will particularly interest investigators who regard human actions or utterances as a necessary part of their data, those with a general interest in the nature and scope of scientific thought should also find it rewarding. The contributions represent

a coherent tradition of inquiry in areas too abstract and complex for easy intelligibility, but lucid writing, with a minimum of esoteric terminology, comes close to eliminating the difficulties involved.

The central issue is how social scientists should formulate a general strategy for understanding and explaining human beliefs and actions. Such a strategy, it is agreed, must take account of the subjective, meaning which distinguishes "action" from "behaviour". Compare a human being seeking money with a rat seeking food. The desire for money becomes intelligible only through its meaning—its subjective significance in a wide range of social relationships. So for beliefs and actions in general; they can be understood only contextually, as elements in meaningful systems; particular beliefs are intelligible only in so far as the total context of belief is intelligible.

This raises important problems concerning the degree to which mutual understanding is possible between any set of actors. It is in the work of social anthropologists, however, that these problems emerge with particular clarity, and the understanding of alien cultures consequently provides the principal subject of discussion here. How can we know when the meaning of an alien utterance has been captured in our own language? To what extent can the properties of alien belief systems be assumed to resemble our own? And what is to be made of beliefs which seem to us self-evidently false, contradictory or otherwise irrational?

With respect to this last question, two basic positions can be identified. One accepts the existence of "irrationality" and seeks to account for it as such: it is the product of bias, or of a mistaken world view, or illogicality: it persists in a culture because social norms discourage rational criticism, or because scientific method is not available to refute it. The other holds that seeming irrationality can become intelligible if its relationship to its context is more closely scrutinized: if beliefs are given significance only in relation to those actions with which they are concretely associated, their "irrationality" may disappear or become irrelevant: if contextual evidence can make a metaphorical or symbolic interpretation of beliefs plausible then, again, all is well.

The intensity of this conflict unfortunately obscures the fact that the two positions are not mutually exclusive. Irrational or false beliefs, as here defined, are endemic in all societies, and it is hard to apply symbolic explanations everywhere (consider, for example, the "irrationality" which these authors painstakingly demonstrate in each other's work). On the other hand, to interpret

the Nuer belief that human twins are birds as symbolism is at least more promising than to treat it as a curious empirical error. Moreover, it is not difficult to combine the approaches: given that there are many ways of being "irrational", symbolism can help to explain why particular examples occur in particular contexts.

Both approaches assume that "irrational" beliefs need different explanatory treatment to "rational" ones, and hence that it is, in principle, possible to distinguish the two by external objective standards. But, in spite of its title, the book does not give this topic detailed consideration; "irrationality" is usually the starting point for analysis, not its product. Crude models of rationality, usually drawn from the philosophy of science, serve as a sketchy backdrop to the problems already discussed. Empiricism lies behind puzzlement at the incidence of false beliefs. Popper's philosophy is linked with interest in why alien actors hold beliefs uncritically. (Unfortunately, P. Winch relates his "all is rational" view of alien belief systems not to T. S. Kuhn but to their common precursor Wittgenstein, thus spoiling the pattern!)

What does emerge is that if objective criteria of rationality exist there is at present no hope of a consensus on what they are. It could in any case be argued, against the dominant approach in this volume, that such criteria are of little interest to the practical investigator. If he must account for the existence of "false" beliefs, he must do no less for "true" ones; if dogmatic adherence to beliefs is problematic, so too is open-mindedness and provisional commitment. Much of the discussion in this volume could be reformulated to apply to the aetiology and ecology of all beliefs, and merely loses perspective by being confined to the analysis of "irrational" residues. Robin Horton's admirable comparison of African traditional thought with that of Western natural science demonstrates the value of widening the scope of the debate, treating our own beliefs with genuine curiosity.

I would agree that any paradigm of rationality must be broadly compatible with the procedures of the natural sciences. Given the rich variety of scientific thought, however, and the way it consistently eludes any single formal description, I am led to adopt what Gellner would call a "charitable" view of alien belief systems, based on the weakest possible rationality criteria. Those who would use stronger or more objective ones should consider, among other things, how much of modern science they would thereby define as irrational. This position comes closest to that of Winch, who nevertheless misuses his own arguments. By treating all belief systems as

rational, he does not show that beliefs are immune to causal explanation, but that the same forms of causal analysis can be universally applied to all beliefs—something not yet fully recognized, at least within the social sciences.

S. B. BARNES

Natural Selection

Coefficients of Natural Selection. By L. M. Cook. (Biological Sciences.) Pp. 207. (Hutchinson University Library: London, February 1971.) £2.50 boards; £1.25 paper.

THE problem of explaining mathematical arguments to biologists has driven many a promising teacher to despair. The biological undergraduate, and occasionally even the graduate, is prone to go into shock when faced with an algebraic equation as complex as

$$a = \frac{bc}{d} \quad \text{Nowhere is the problem more}$$

acute than in population genetics, where the underlying arguments are largely mathematical but the observations and experiments are firmly based in natural history. Dr Cook has attempted the dreadful task of bridging the chasm between them, and he has largely succeeded.

His book is neither a text for undergraduates, although there are many who would benefit from it, nor an account of methods in research. It is a stimulating, original and idiosyncratic essay about the genetic analysis of natural and experimental populations. He leads his readers gently through the complexities of selection differentials, the calculation of equilibria, and the analysis of selective forces depending on gene-frequency and population density. At times, understandably, he falls into the trap of rendering an argument more obscure by explaining it too much. Less often, but more seriously, the reader may be led astray by misprints (as on pages 29, 43 and 44) or other errors (as on pages 59, 142 and 160). There are some surprising gaps. For example, he chooses to discuss the phenomena of non-random mating without mentioning the work of Ehrman or Spiess.

These are matters, however, that can be remedied if, as devoutly we may wish, the book reaches a second edition. Its virtues far outweigh its vices. An example of these virtues, to a statistically naive reviewer, is a uniquely lucid exposition of the method of maximum likelihood.

I believe that the value of the book will prove to be inversely proportional to the mathematical ability of the reader. It should be welcomed by biologists and neglected by mathematicians.

BRYAN CLARKE

Food and Safety

Metabolic Aspects of Food Safety. Edited by Francis Roe. Pp. xxiii+612. (Blackwell: Oxford and Edinburgh, 1970.) £7.

ABOUT ten years ago the Nuffield Foundation became concerned with the toxicological risks associated with the increase in chemical and physical treatment of food. To evaluate the hazards involved it is necessary to work with small laboratory animals, but lack of knowledge of their diseases made the investigations difficult. In 1966 the first food safety conference led to the publication of a useful book, *The Pathology of Small Laboratory Animals*. In 1969 the second food safety conference considered the tests used to assess the safety of food additives and contaminants, and the problems that arise in interpretation of experimental results. It is not as easy as might be supposed to decide whether a compound is toxic to an animal even in the conditions of the experiment, without the additional problem of extrapolation to a human population and the conditions in which the compound is or could be consumed. As toxicology is studied by physiologists, biochemists and electron microscopists, there was a need for different people concerned to meet to discuss the problems. The book of the conference is disappointing, although it should be of some use to those engaged in this work.

"Metabolic Aspects" is a very misleading title, as the book is not concerned chiefly with the metabolism of food constituents, additives or contaminants, or with their effects on metabolism of the animal. "Biological Aspects" would have been more appropriate. A very heterogeneous collection of twenty articles discusses basic physiology of the small intestine and of gastrointestinal absorption, renal function tests in animals and in man, and the significance of such factors as gut flora, age, sex, hormones and nutritional status of the experimental animal. The fact that protein deficiency makes animals less sensitive to compounds such as heptachlor which exert their toxic effects after metabolism, and more sensitive to compounds such as aflatoxin, the toxicity of which probably does not depend on their metabolic conversion, underlines the difficulty of applying results both to the affluent society and to the undernourished countries.

One basic problem is whether any effect produced by a chemical should be regarded as evidence of toxicity, even if it does not apparently inconvenience the animal. Thus many food additives cause an increase in liver weight, and the problem of whether this is harmful or possibly even beneficial is discussed. Obviously to assess the significance of the increase in liver weight caused by

chemicals it should be compared with changes occurring naturally. However, in the present context, the long detailed discussion of the increase in liver weight occurring during pregnancy and lactation seems out of place, in the absence of sufficient comparison with chemically induced enlargement. Only a shrewd question in the discussion brought out a fundamental difference: chemical-induced liver enlargement is frequently accompanied by hypertrophy of the smooth endoplasmic reticulum, that occurring during reproduction is not. The important question of the reversibility of natural and chemically induced changes is barely mentioned. The problem of whether an increase in weight is harmful leads to the question of what controls liver weight, and of the mechanism by which the changes are brought about. Thus it is essential "to find out not only what happened but how it happened" and to study the basic biochemical processes before the results of toxicity tests can be evaluated. Two good chapters get to grips with the problem in this way. One discusses metabolic aspects of liver tumour induction in animals by compounds known or suspected to be food contaminants, and the other discusses the ultrastructural changes.

Although apparently the aim of the book is to have a wide scope rather than to study any particular problem in depth, there are some important omissions. There is no mention of possible hazards to the brain, although the vulnerability of the central nervous system had been demonstrated spectacularly and tragically ten years before, when methyl-mercury contamination of fish was shown to be responsible for Minamata disease in Japan. More surprisingly teratogenesis is not discussed, although dyes, fungal metabolites and other possible food contaminants are known teratogens. The basic physiology, biochemistry and tests of kidney and liver function in man, are dealt with in standard textbooks. If these subjects could have been replaced by discussion more directly relevant in the present context, the book could have gone much further into the problems and would have been a more valuable contribution to the subject.

V. M. CRADDOCK

Tsetse and Ecology

The Role of the Trypanosomiasis in African Ecology: a Study of the Tsetse Fly Problem. By John Ford. Pp. xiv+568. (Clarendon: Oxford; Oxford University: London, March 1971.) £6.50.

THE change of title of the East African Tsetse and Trypanosomiasis Research and Reclamation Organization

(EATTRRO) to East African Trypanosomiasis Research Organization (EATRO) in 1956 signified a change of approach—from one in which the prime emphasis was on the insect vectors of trypanosomiasis—*Glossina* (tsetse flies)—to a more balanced one in which medical, veterinary, entomological and ecological aspects were to be studied as a whole. Also, the first organization was concerned with both research and reclamation, the second solely with research. John Ford served for many years with the earlier organization, only briefly with EATRO, as director, until he went to Rhodesia as director of tsetse control in 1957. He is primarily an entomologist, but a very thoughtful one, and his book is a fine attempt to put *Glossina* in proportion among the many other ecological factors which affect the African scene. This is a very different approach from that of the generality of British glossinologists, which was that the elimination of *Glossina* was a certain way of controlling trypanosomiasis; that this should be stressed to the near exclusion of all other approaches; and that economical control consistent with the poverty of the African territories affected should be able to be attained by minor interference with the *Glossina* vegetational environments—if only the ecology of these flies were sufficiently understood.

After extended experience of this approach in East Africa, Ford worked in Rhodesia where game elimination as a *Glossina* control measure had been particularly practised. He subsequently visited and studied in West Africa. He has, therefore, a unique first hand acquaintanceship with three different African regions, all sharply affected by trypanosomiasis, but in different ways. The description of trypanosomiasis situations in these three regions form the core of the book. After five introductory chapters giving essential basic information about the organisms concerned—trypanosomes, *Glossina*, animals and man—Ford devotes nineteen chapters to describing five sample areas, three in East Africa and one each in Rhodesia and in Nigeria. He ends with two summarizing chapters, one considering trypanosomiasis in its continental ecological aspects, the other proposing a new approach.

Basically, Ford's thesis is that, before the advent of the Europeans in Africa, the indigenous peoples had made very considerable advances towards overcoming the obstacle of trypanosomiasis by physiological and cultural adjustments in themselves and in their domestic stock and that this fact is usually overlooked. He considers the epidemics of trypanosomiasis in man and animals since the turn of the century to be direct results of the political and ecological aspects consequent on

European colonization, which acted particularly by disturbing the uninhabited no man's land (*Grenzwildnisse*) which separated tribal areas and kingdoms and which provided mechanisms for adjustment between different tribal groups and with their environment.

Ford marshals an impressive amount of information to support his thesis, delineating the development of affairs in all his five areas. The reader new to the field may find the diversity of the material bewildering, including, as it does, geology, palaeontology, historical fragments, excerpts from the diaries of early travellers, oral tradition, geographical description, entomology, and human and animal demography, all developed together with great profusion of detail so that any individual body of data is difficult to isolate, examine and assess. Nevertheless, the result is of great interest and, whether one agrees or not with Ford's thesis, the book will always be valuable, if only for the amount of data, otherwise difficult to obtain, amassed within it.

In his final chapter, Ford is apprehensive of epidemiological upsets at the termination of the colonial empires as profound as those which attended their establishment and cites present indications from the Congo and the Sudan. He emphasizes, again, the need to relate disease control to expected economic growth rate. He urges the development of the mathematical epidemiology of trypanosomiasis. He laments the neglect of entomologists to study, at the same time as the habits of their insects, also the habits of the people and the animals bitten. He hopes for a better balance under political freedom than has happened under colonial rule. This is questionable and indeed, under the more general approach to trypanosomiasis study in recent years, this lack has been realized and much done to repair it. To my mind, however, much of the uncertainty and misapprehension in the field of trypanosomiasis does indeed derive from the paucity of integrated studies. Trypanosomiasis contrasts sharply in this respect with some other tropical diseases, such as yellow fever, in which integrated teams fairly rapidly worked out the main essentials of the epidemiology, in both South America and Africa.

Considerable progress in integrated studies was indeed made by the East African Trypanosomiasis Research Organization and is indeed still continuing in spite of the dislocation caused by the loss of long-experienced personnel consequent on the granting of independence to East African territories in 1962–63.

The book is well illustrated with line diagrams and is fully indexed. There is a bibliography of some 600 sources.

W. H. R. LUMSDEN

Molecular Pharmacology

Essentials of Molecular Pharmacology: Background for Drug Design. By Andrejus Korolkovas. Pp. xv+339. (Wiley Interscience: New York and London, November 1970.) 160s.

THE term molecular pharmacology is of recent currency but may be taken to indicate a new determination among pharmacologists to account for the nature and specificity of drug action in terms of a detailed description of events at the atomic level. Speculation at this level has of course been rife for years but hard facts have been few, and it is really the arrival of new techniques, notably X-ray crystallography of proteins, that have given a great new impetus to this challenging subject. This book deals with the major areas of activity so far including adequate accounts of intermolecular forces and the analysis of chirality. The account of drug-receptor interactions is imaginative and stimulating, but it is here that the weaknesses in contemporary pharmacological arguments become so clear—the argument is based on analogy with enzyme-substrate interactions (themselves not understood unequivocally), and extrapolations from structure activity studies.

The position is rapidly developing where drug binding directly to receptors is possible so that the analogies may be put aside, but as the X-ray studies of binding of enantiomeric glycosides to lysozyme, and isomeric nucleotides to ribonuclease have shown, changes in structure of the ligand may entail a major change in the geometry of the complex that cannot be predicted from structure activity studies. The implication is that structural techniques, particularly X-ray crystallography and nuclear magnetic resonance, must be decisive tools for the molecular pharmacologist.

The theories of drug action discussed in this book are bound to become rapidly clarified as the study of isolated receptors proceeds. It is interesting to see how history repeats itself. The isolation and crystallization of enzymes was inhibited by vitalistic concepts, the isolation of receptors was similarly inhibited by beliefs that receptors could not survive isolation from their environment in membranes; lo and behold, when isolated they are as tough as old boots. Nevertheless, we must not be carried away by excessive optimism, isolation of receptors will not answer all the questions of drug action any more than isolation of enzymes solves the problem of how enzymes work, but it does have the enormous advantage of replacing mystery by tangibility.

For the rapid development of molecular pharmacology that is now just beginning, this book provides a useful

and interesting primer that can be strongly recommended.

A. S. V. BURGEN

Complex Chemistry

Organometallic Chemistry. Edited by F. G. A. Stone and M. I. Bruce. (Plenary Lectures at the Fourth International Conference on Organometallic Chemistry, held at Bristol, UK, July 28–August 1, 1969.) (International Union of Pure and Applied Chemistry in conjunction with the Chemical Society, London. *Pure and Applied Chemistry*, Vol. 23, No. 4, 1970.) Pp. 375–503. (Butterworth: London, 1970.) £3.50.

PUBLICATION, in a hard-cover version, of the proceedings of symposia of the International Union of Pure and Applied Chemistry has complemented, for the past few years, their normal appearance in the journal *Pure and Applied Chemistry*. One would not have guessed that such a double-barrelled approach would have been profitable for the publishers—it must be a tribute to the balance and high quality of reviews which appear in this volume and in its predecessors.

So far, the only characterized organometallic complex occurring in nature is vitamin B₁₂, and its chemistry is better understood now through the systematic studies of metal complexes of porphyrins, corrins and corroles. These are reviewed by A. W. Johnson. K. Schlögl concentrates his attention on chirality in the metallocenes and the summary serves as a general reminder that the optical activities of organometallic catalysts and stereospecificity of polymerization reactions could be a renewed focus of interest in the near future. Gubin surveys the information which electrochemical methods have given on energy levels and bonding in the metallocenes and cyclopentadienyl metal carbonyls and Chini completes our exposure to transition metal chemistry by a succinct summary of the chemistry of a number of carbonyl clusters of the iron and cobalt triads.

It is good to see main group organometallic chemistry so well represented. Brown gives a particularly nice account of nuclear magnetic resonance studies of structure and exchange reactions of organolithium compounds; Seyferth summarizes insertion reactions of methylene bridges into group IV hydrides and halides while Neumann emphasizes the free radical chemistry of organotin compounds.

Obviously, individual volumes can have no claim to comprehensiveness but together they represent a most valuable addition to the secondary literature.

R. MASON

CORRESPONDENCE

Metric Chains

SIR,—You chose an unfortunate subject for your aside upon shortening cricket pitches “. . . (. . . a non-metric measure—who now knows what a chain is?)”¹.

It is unfortunate that, with the impending change to the metric system, we do not much use chains and furlongs and even the infamous rod, pole or perch, for they correspond respectively to 20 m, 200 m and 5 m with an accuracy of 0.6%.

Yours faithfully,

S. D. STEEL

*Department of Inorganic,
Physical and Industrial Chemistry,
Donnan Laboratories,
Grove Street,
PO Box 147,
Liverpool L69 3BX*

¹ *Nature*, 232, 433 (1971).

Telescope Administration

SIR,—Twice each year your advertisement pages invite applications for observing time on the Isaac Newton Telescope. Lest any potential applicant be deterred by the “widespread feeling” noted in your editorial (*Nature*, 232, 289; 1971) that the Royal Greenwich Observatory exerts a detrimental influence on the running of this telescope, perhaps you would allow an informed comment.

If “running” refers to the day-to-day management and maintenance of the telescope, then indeed any neglect here would, as stated, be inimical to the progress of British astronomy. But if this is what is alleged, the proper place to complain is on the spot at the time. No such complaints are in fact made by visiting observers, and those responsible for the care of the telescope must be forgiven if they decline to notice anonymous allegations by others, especially when they are wholly unsupported by facts.

If, however, the criticism is now, as it has been in the past, of the observatory's alleged monopoly in the design and construction of ancillary equipment, it is time to reiterate that no such monopoly exists. Any successful applicant for observing time may bring his own equipment—many of them do—and the only requirement is that it shall be compatible with the telescope itself. As to the larger spectrographs, it is true that these are of RGO design. It is equally true that had the Astronomer Royal not taken the initiative to get them built, no spectrographs for common use would now exist. It is this situation that would indeed have

been inimical to the progress of British astronomy.

But maybe the rub lies in the allocation of observing time. This is done twice a year by a Science Research Council panel of six working astronomers, not all of them in the optical field and only one from the Royal Greenwich Observatory. Selection among the applications received is strictly according to the scientific merit of the programmes proposed, and I am sure the members of the panel would repudiate any suggestion that they unduly favour RGO applicants. It is true that RGO applications are in fact awarded more time than any others; but they are in a substantial majority and the panel plainly adjudges them more worthy of support.

If there are those who find the basis of allocation unfair, let them suggest a more equitable one. If they allege sinister influences by the major applicants on the process of allocation, let them produce something more substantial than hints in the scientific press.

Yours faithfully,

A. HUNTER

*Secretary, Large Telescope Users' Panel,
Royal Greenwich Observatory,
Herstmonceux Castle,
Hailsham, Sussex*

SIR,—Your article on “New Astronomy” (*Nature*, 232, 289; 1971) was informative and interesting. Before commenting on points of substance, however, may I correct one misunderstanding which the article revealed?

I refer to the “widely held” criticism, attributed to “many astronomers” who see the RGO as a “white elephant”—on the grounds, according to you, that the £1.2 million which the SRC spends on the RGO, the Royal Observatory Edinburgh and on the observatories in South Africa, gives poor returns compared with the running costs of the Hale Observatories of \$1.7 million a year.

The Hale Observatories are not government observatories and have no national responsibilities. They spend nothing on the equivalent of the Nautical Almanac Office, the Time Service and the Meridian and Astrometry Departments of RGO which take up some 57% of the total RGO budget. If you then compare the remaining 43% of the RGO budget, plus the full cost of the South African Observatories and the Royal Observatory Edinburgh, the total comes out for all practical purposes the same as the cost of the Hale Observatories—in round figures, £700,000.

You were, of course, right to draw attention to the disquiet of the scientific staff of the RGO about the future of their scientific work. In part, the bad staff relations in the Science Research Council are a cause of this. The fact that they were given a categorical assurance that they would be consulted about any proposal that the Astronomer Royal post would be divorced from the directorship of the RGO, but nevertheless were not consulted about it at all, is only an unusually dramatic illustration of why the management is losing the confidence of its staff. Nor does the explanation which has now been given make things any better.

But it is the affair of the Northern Hemisphere telescope which has caused the greatest anxiety. As you point out, there have been powerful pressures in favour of creating a third administrative centre in the UK for the Northern Hemisphere telescope. This should be a scientific and administrative responsibility of the SRC as such, one of whose responsibilities it is to provide facilities for common use by a variety of university scientists. The logical site for the centre is at the RGO—or, alternatively, at the Royal Observatory Edinburgh—but it appears as if there has been tremendous opposition to this. To establish one university rather than another as a third centre for the handling of common facilities would surely be contrary to the purpose of the SRC, as well as being unnecessarily costly; and there is no point in having a third centre all by itself.

It is also the function of the SRC to do its own research at its own establishments, and a considerable number of first-rate scientists are employed on its staff for this very purpose. Collaboration with universities in the use of scarce facilities and equipment held in common by the SRC is fully accepted by the staff and by the institution. It is one of the purposes of SRC to bring about this collaboration, and such differences as there may be from time to time between the SRC's own scientists and those from universities should be concerned with nothing more than matters of balance. The affair of the Astronomer Royal has raised the question, however, of whether it is a question of balance. The policy of the Science Research Council is in the hands of the majority of university representatives on the council, and in a period in which there is keen competition for the relatively limited amount of money available, the SRC's own scientists are looking for reassurance about the long-term standing of their own research work.

Not only are they not getting it, but they can see no means by which, within the SRC as it stands, they can right the balance if it tips too much in the universities' direction.

Yours faithfully,

JOHN LYONS
Deputy General Secretary.

*The Institution of Professional Civil Servants,
Northumberland Street,
London WC2*

Orbital Planes of Planets

SIR,—Recently (April 26) we attended a lecture at the University of the South, Sewanee, Tennessee, by Dr Peter Van de Kamp of Sproul Observatory, Swathmore, Pennsylvania. He spoke on "The Search for Extra-Solar Planets", his work for 35 years, which indicates that Barnard's star has two planetary companions bearing a similarity to Jupiter and Saturn.

This lecture restimulated an idea held by one of us (Wells) for several years. We know the ecliptic plane is practically at right angles to the plane of the galaxy,

but we don't know if this is only by chance or of deep significance. After the lecture Dr Van de Kamp was asked if enough was known about the orbits of stars with companions to determine orbital planet orientation. He said he had not considered it but some work might well be devoted to the question. He commented on the planes of binaries as being apparently random.

During the 70 mile drive home, we discussed this further. It was decided that, since Dr Van de Kamp had not investigated this relationship, it may not ever have been properly considered.

It seems that one of the most fundamental bits of information that could come of extra-solar planet searches would be a determination of the distribution of orbital planes. If other solar systems besides ours should be found with the orbital planes also at right angles it would be suggestive, with probable implications for galactic evolution, as indeed would any significant deviation from random orientation of orbital planes.

Should a preferred orientation be established, it could have a great bearing on theories of galactic dynamics. It

would seem that our solar system may have been formed approximately 90° from the present galactic location initially, since difficulties are foreseen in trying to reconcile the ecliptic angle with fluid mechanics or condensation theories.

If we should be able to determine the plane of other ecliptics around other stars, it would greatly simplify the search for extra-solar planets by determining the directions from the stars to expect planets; a great advantage in radio astronomy or other scanning methods. For instance, Project Ozma was apparently limited in scan directions.

It was felt that this letter might bring comments from others on this question and help keep it before the attention of astronomers who might be able further to evaluate and pursue the phenomena.

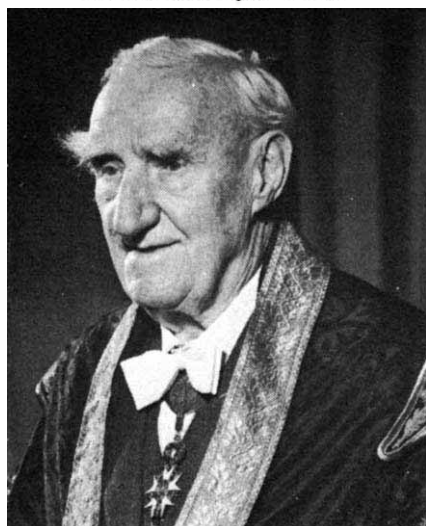
Yours faithfully,

ERNEST H. WELLS
DANIEL PAYNE HALE

*National Aeronautics and
Space Administration,
George C. Marshall Space
Flight Center,
Huntsville, Alabama 35812*

Obituary

Lord Boyd Orr



LORD BOYD ORR of Brechin Mearns, Nobel Peace Laureate, Chancellor of the University of Glasgow, first director-general of the United Nations Food and Agricultural Organization, first director of the Rowett Research Institute and founder of the World Food Council, died on June 25 at the age of ninety.

John Boyd Orr was a graduate in arts, science and medicine of the University of Glasgow, where he also obtained his MD and DSc. His first external appointment was to a new research post in Aberdeen linked to the College of Agriculture and the

university. This subsequently grew into the Rowett Research Institute. However, before he could get established the First World War began. Until 1917, he served with the RAMC, winning the DSO and MC with bar. Later he undertook an investigation of the physical requirements of servicemen for the navy.

Some of his first experience in nutritional investigation was gained in collaboration with the late Professor E. P. Cathcart at Glasgow. Here he worked chiefly on water and protein metabolism and on energy expenditure during work. There he was influenced by research on the diet of the working classes. On moving to Aberdeen, he took the advice of Cathcart and studied the mineral metabolism and needs of farm livestock, developing both topics with characteristic energy and insight. Some of his most impressive work was on mineral deficiencies and soil exhaustion in relation to pasture production both at home and abroad. This led him to establish a clinical unit to investigate the effects of husbandry techniques on the human populations of Masai and Kikuyu. It also established his interest in nutrition and disease and their interrelations.

He was responsible for great improvements in the production of meat, wool and milk, and helped to bring prosperity to the livestock industry. He gave the farmer more precise

knowledge in the selection of food mixtures as a substitute for growing pastures, particularly in the wintering of his stock. He also gave some definition to the biochemical and immunological changes which precede and accompany the general symptoms of disordered metabolism caused by nutritional deficiency or imbalance. After starting work at the institute in a cellar of Marischal College, Orr received the financial backing of such men as Dr John Quiller Rowett (after whom the institute was named) and was able to establish at the institute the Imperial Bureau of Animal Nutrition.

Orr's professional concern was with animals of agricultural importance, but he found that whereas he had no difficulty in persuading farmers of the value to their stock and pockets of the application of sound nutritional principles, he could not convince anyone that the same was true of children. At that period the nutrition of man himself was an art rather than science, empiricism rather than experimentation, general impressions rather than controlled observation. But now, the newer knowledge of nutrition was growing, requirements could approximately be defined, and dietary surveys could expose the gap between requirement and that consumed. A large scale demonstration of the nutritious value of milk for school children partly done to promote the increased consumption

of milk for the benefit of the dairy industry, but primarily done to promote the health of the children whom he suspected of being undernourished, led to further work on human nutrition. With government financial help he undertook the survey which became a classic: *Food, Health and Income*, and was first published in 1936 and had world-wide repercussions.

Then there followed the more extensive dietary and clinical surveys of representative groups of families with children of varying income levels in many parts of Britain, which further demonstrated the relation of food, health and income, and the consciousness of this on a world scale grew into a natural and later international food policy based on human needs. This was supported by Carnegie UK Trust funds. Such was the value of this

accumulated knowledge of human needs and intakes that Orr was able to so advise the Government on the scientific food policy during World War II that we were able to emerge in a better nutritional state than when we entered, for rationing was based on needs and not on purchasing power. Further, these observations and knowledge displayed by Orr so impressed the United Nations that Sir John Orr—as he then was, having been knighted in 1935—was appointed at the Quebec Conference the first director-general of the Food and Agricultural Organization, coinciding with his retirement from the Rowett Research Institute in the autumn of 1945, and this post he held until 1948. It was on the platform or at the conference table that his biggest personal impacts were made.

He was lean with craggy eyebrows,

long jawed, and although he had no tricks of oratory, the single-mindedness of his argument—one thing at a time—and his prophetic sincerity generally won the day. Some thought him naïve, but it was an expressed simplicity with a purpose. His hunches were very sound: he was sometimes impatient of the slowness of the research worker to corroborate what he felt in his bones to be valid and vital.

Orr inherited much of his strength of character from his mother, who was a Boyd. In 1915 he married Miss Elizabeth Pearson Callum, of West Kilbride. They were seldom separated and travelled the world together. She was a wonderful partner and ambassador. He is survived by his wife and two married daughters. Their only son was killed on a Coastal Command mission during the war.

Announcements

International Meetings

September 15–17, **British Society for Cell Biology Meeting**, Bristol (Dr J. M. N. Boss, Department of Physiology, Veterinary School, Park Row, Bristol BS1 5LS).

September 20–21, **Small Craft**, Southampton (Royal Institution of Naval Architects, 10 Upper Belgrave Street, London SW1X 8BQ).

September 21–23, **Infrared Techniques**, Reading (Conference Department, Institution of Electronic and Radio Engineers, 8–9 Bedford Square, London WC1B 3RG).

September 28–29, **Biochemistry, Genetics and Therapy of Schizophrenia**, London (Schizophrenia Association of Great Britain, Llanfair Hall, Caernarvon).

September 28–29, **Ultrasonics 71**, London (Mr A. H. Crawford, Ultrasonics 71, 32 High Street, Guildford, Surrey).

October 11–12, **Natural Slopes Stability and Conservation**, Naples and Cosenza (Dr G. Guzzetta, Istituto di Geologia, Naples, Italy).

October 18–22, **Eurocon 71**, Lausanne (Eurocon 71 Office, 24 Chemin de Bellevue, CH-1007 Lausanne, Switzerland).

November 10, **Medical Thermography**, London (Warren Cook & Partners, Woodfield House, Goudhurst, Kent).

November 11–12, **Coatings**, Great Malvern (M. G. Bader, Department of Metallurgy and Materials Technology, University of Surrey, Guildford, Surrey).

November 11–12, **Endocrine and Non-endocrine Hormone Producing Tumours**, Houston (Mrs Jane Brandenberger, Information Coordinator, University of Texas M.D. Anderson Hospital and Tumor Institute, Texas Medical Center, Houston, Texas 77025, USA).

Reports and Publications

not included in the Monthly Books Supplement

Other Countries

Australian Journal of Zoology. Supplementary Series. Supplement No. 1: The Tipulidae (Diptera) of Australia. 3: The Genus *Psilopyga* Westwood. By N. V. Dobrotworsky. Pp. 41. (East Melbourne: CSIRO, 1971.) [195]

Australian Academy of Science. Reports No. 13: Education and the Environmental Crisis. (Proceedings of a Conference held in Canberra, 24–26 April 1970 under the auspices of the Australian Academy of Science through its National Committee for the International Biological Programme.) Edited by Jeremy Evans and Stephen Boyden. Pp. 117. (Canberra: Australian Academy of Science, 1970.) [195]

Evaluation of Food Additives: Specifications for the Identity and Purity of Food Additives and their Toxicological Evaluation—Some Extraction Solvents and Certain other Substances; and a Review of the Technological Efficacy of some Antimicrobial Agents. (Fourteenth Report of the joint FAO/WHO Expert Committee on Food Additives, Geneva, 24 June–2 July 1970. FAO Nutrition Meetings Report Series, No. 48. WHO Technical Report Series, No. 462.) Pp. 36. (Rome: FAO; London: HMSO, 1971.) 30p; \$1. [205]

National Academy of Engineering—Committee on Public Engineering Policy. Federal Support of Applied Research. Pp. 16. Priorities in Applied Research: an Initial Appraisal. Pp. 33. (Washington, DC: National Academy of Engineering, 1970.) [215]

Mercury in the Environment—The Human Element. By Robin A. Wallace, William Fulkerson, Wilbur D. Shults and William S. Lyon. (ORNL-NSF Environmental Program. ORNL NSF-EP-1.) Pp. vii+61. (Oak Ridge, Tennessee: Oak Ridge National Laboratory, 1971.) [215]

HOW TO BUY NATURE

Volumes start in January, March, May, July, September and November, but subscriptions may begin at any time.

The direct postal price per subscription is:

12 MONTHS* (52 issues per title)

	Surface Mail UK and worldwide	Airfreight U.S.A. Canada
Nature (Friday)	£14	\$48 \$52
Nature + Nature Physical Science	£24	\$83 \$90
Nature + Nature New Biology	£24	\$83 \$90
All three editions	£29.50	\$108 \$116
Annual Index	£1	\$3 \$3

* Rates for shorter periods *pro rata* (minimum three months)
(Charge for delivery by air mail on application)

Editorial and Publishing Offices of NATURE

MACMILLAN JOURNALS LIMITED
4 LITTLE ESSEX STREET, LONDON WC2R 3LF
Telephone Number : 01-836 6633. Telegrams : Phusis London WC2R 3LF

711 NATIONAL PRESS BUILDING
WASHINGTON DC 20004
Telephone Number : 202-737 2355

Subscription Department
MACMILLAN JOURNALS LIMITED
BRUNEL ROAD, BASINGSTOKE, HANTS
Telephone Number : Basingstoke 5431

American display advertisements
NATURE SCIENTIFIC PUBLICATIONS INC
711 NATIONAL PRESS BUILDING
WASHINGTON DC 20004

All other advertisements
T. G. SCOTT & SON, LIMITED
1 CLEMENT'S INN, LONDON WC2A 2ED
Telephone : 01-242 6264/01-405 4743
Telegrams : Textualist London WC2A 2ED

Registered as a newspaper at the Post Office

Copyright © Macmillan Journals Limited, August 20 1971